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METASTATIC TUMORS OF THE JAWS

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EARLY diagnosis and treatment of malignant lesions of the oral cavity and jaws are of prime importance. Primary malignant tumors that occur in accessible regions and that display certain recognizable characteristics usually do not present a diagnostic challenge to the competent and informed dentist or physician. Recognition of metastatic tumors in the bones of the jaw is more difficult for a number of reasons, namely, (1) they are uncommon, (2) they often are located centrally and produce nonspecific signs and symptoms, such as pain, swelling, and loss of sensation only late in their course, (3) roentgenologic changes may be minimal or absent and are often nonspecific, and (4) the metastatic tumor in the jaw may be the first evidence of an unrecognized primary tumor in another part of the body.

Metastatic malignant tumors of the jaws from distant primary sites have been diagnosed erroneously as infections of dental origin, various types of cysts, local traumatic conditions, osteomyelitis, benign tumors, and primary malignant tumors. Inappropriate management often follows such misdiagnosis.

CASE REPORT

A 48-year-old woman came to the Mayo Clinic because of a painless gingival swelling of approximately six weeks' duration in the region of the mandibular left lateral incisor. On the first of six visits to her home dentist, the lesion was diagnosed as an infectious process and was treated with "some strong drug for mouth infection." This treatment being ineffective, the patient was instructed at different times to use hydrogen peroxide, salt, and bicarbonate of soda in the form of mouthwashes. On at least two different occasions, the swollen gingival tissue was ineffectually excised but not subjected to pathologic study.

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Possibly unbeknown to her dentist, the patient had undergone a left nephrectomy and partial ureterectomy for hypernephroma (adenocarcinoma of the kidney) three and one-half years prior to the onset of these mandibular symptoms. Six months before the onset of oral complaints, she was hospitalized because of recurrent episodes of fever. Clinical and roentgenologic examinations at that time demonstrated an upper abdominal mass behind the stomach which was considered to be a recurrent hypernephroma and was treated by irradiation. Later, thoracic roentgenograms revealed metastatic lesions in both lungs.

Examination at the clinic disclosed a soft, deep-red, hypertrophic, interdental papilla, covered by a whitish membrane, between the mandibular cuspid and the lateral incisor on the left. This appearance and the roentgenograms that demonstrated a zone of radiolucency suggested a vascular epulis or a "peripheral fibroma" in the alveolar crest adjacent to the lateral incisor and cuspid teeth.

Three days later the mandibular left lateral incisor was extracted, the enlarged interdental papilla was excised, and the alveolar bone and remnants of periodontal membrane were removed. Pathologic study revealed the presence of a metastatic renal carcinoma. The patient died within a few weeks, with metastases to the skin and central nervous system.

Such cases as this emphasize the necessity of giving increased attention to the problem of metastatic tumors of the jaws.

PRESENT STUDY

A study was made of the records of all cases seen at the Mayo Clinic from 1911 through 1957 in which malignant lesions of the jaws were present and in which metastasis from a recognized or unrecognized primary source was considered as even a possibility. The records of 594 such cases were reviewed in detail. This initial screening netted sixty-three cases in which the evidence was sufficient to warrant further investigation. Every attempt was made to distinguish between cases of actual metastasis to the jaws from distant primary sources and those in which the jaws were involved primarily or secondarily by malignant tumors of contiguous structures. Therefore, it was necessary to establish definite criteria for lesions included in this study. These criteria were (1) pronounced histologic resemblance to a known primary tumor at another location, (2) strong clinical and histologic evidence of metastasis from a primary source not definitely proved but strongly suspected, and (3) lack of resemblance of the suspected metastatic lesion to primary tumors that arise in the jaws themselves.

Many of the lesions suspected of being metastatic in nature were squamous-cell carcinomas located in the jaws at sites that could not be explained readily on the basis of direct extension, although primary carcinomas of the lip or face had been present. To maintain intellectual honesty, it was impossible to exclude these lesions from this study. Consequently, the following additional criteria applying only to squamous-cell carcinoma were necessary: (1) Tissue from both the original lesion and the suspected metastatic tumor had to be available for microscopic examination; (2) it had to be definitely established that no ulceration of the gingiva, mucous membrane, or skin which might be construed as a primary tumor was present in the region of the suspected metastatic tumor; (3) microscopic examination of tissue from the lesion had to establish that the lesion was squamous-cell carcinoma rather than ameloblastoma with squamous metaplasia.

Despite strong clinical evidence that metastasis to the jaws had occurred, it was necessary to eliminate forty-three of the sixty-three cases because of their failure to satisfy one or more of the criteria established. These forty-three eliminated cases included possible metastases in thirty-three cases from the lip, seven from the breast, and one from the kidney; a primary source was not determined in one case, and the lesion in the remaining case evidently was an ameloblastoma with squamous elements.

In the remaining twenty cases, histologic and clinical evidence confirmed that the lesions of the jaws were the result of metastasis from sources outside the jaws. Adequate slides were available for microscopic examination in each of these cases. Of the twenty confirmed metastatic tumors, there were five from hypernephromas, five from squamous-cell carcinomas of the lower lip, two from adenocarcinomas of the breast, and two from adenocarcinomas of the sigmoid. In addition, there was one each from adenocarcinoma of the colon, adenocarcinoma of the prostate, adenocarcinoma of the rectum, squamous-cell carcinoma of the skin of the face in the infraorbital region, and squamous-cell carcinoma of the skin of the nose. The final lesion was squamous-cell carcinoma of the right lateral margin of the tongue which had metastasized to the left mandible.

Age.—The youngest patient in this study was 29 years of age and the oldest was seventy-two when seen initially at the clinic. The average age was 56.7 years, and the median was 60 years.

Sex.—Eleven of the patients were men and nine were women. Three of the five hypernephromas occurred in women, as did the two carcinomas of the breast, the two carcinomas of the sigmoid, the rectal carcinoma, and the carcinoma of the skin of the nose. The two remaining hypernephromas, the five carcinomas of the lip, the carcinoma of the skin of the face, the carcinoma of the tongue, the prostatic carcinoma, and the carcinoma of the colon were found in the men.

Signs and Symptoms.—Local swelling occurred in every patient; however, no particular type or degree of swelling was outstanding. It varied from minor gingival enlargement to massive swelling with distortion of normal facial contours.

Pain was not reported as a constant finding. When any mention of sensation was made, the descriptions were varied and inconsistent. Eight patients reported that they had had no pain or change in sensation whatsoever. Three patients complained of a definite aching of the affected jaw, with extension of pain to other regions. Two patients described their pain as arising from teeth, and two had pain of unspecified type or intensity. One man stated that he did not have pain but that he did have a vague tenderness or sensitivity of the jaw. The remaining four patients complained of altered sensation of the lip; one of these four had alternating pain and numbness of the lip, and the remaining three experienced a loss of sensation similar to that produced by a local anesthetic.

The majority of these twenty lesions occurred in edentulous regions. Loosening or extrusion of the teeth was produced by only one of those tumors present in a tooth-bearing region.

Trismus or interference with function of the jaws was observed in six of the twenty cases.

One patient who had metastatic hypernephroma in the mandible presented a rather unusual feature. A definite pulsation could be felt over the swollen portion of the jaw. Auscultation over this region revealed a loud, blowing, pulsating murmur, such as might be produced by an aneurysm. Willis[21] has commented that this feature, although rare, may occur and appears to be restricted to metastatic lesions arising from renal and thyroidal carcinomas.

Fig. 1.—Right side of mandible showing osteoblastic metastatic tumor from adenocarcinoma of the prostate.

Many of the patients could not give an accurate account of when the first signs of involvement of the jaw appeared. Therefore, only an approximation of the duration of the lesions in the jaws could be made. The shortest period reported was three days and the longest was two years. The majority of those patients who could estimate the time of their first symptoms thought that these symptoms had occurred within one month prior to their seeking treatment.

Apparently none of the patients who had undergone previous treatment for carcinomas of other regions of the body related their jaw symptoms to the original tumors.

Location.—The maxilla was involved in only one case. The lesion in this instance, which proved to be a metastatic tumor from a hypernephroma, occurred at the root apex of a maxillary cuspid tooth.

The location of the remaining nineteen lesions could be determined with reasonable accuracy by examination of surgical specimens or roentgenograms of the mandible. Eleven of the lesions occurred in the molar region of the mandible, four were found at the angle or in the inferior portion of the

ramus, and three were in the region of the mental foramen. Only one, a metastatic growth from a hypernephroma, was discovered anterior to the mental foramen in the mandibular cuspid region.

None of the patients had multiple lesions in the jaws.

Roentgenologic Diagnosis.—The roentgenologic appearance of these metastatic tumors of the jaws was extremely variable. No single outstanding characteristic was discovered.

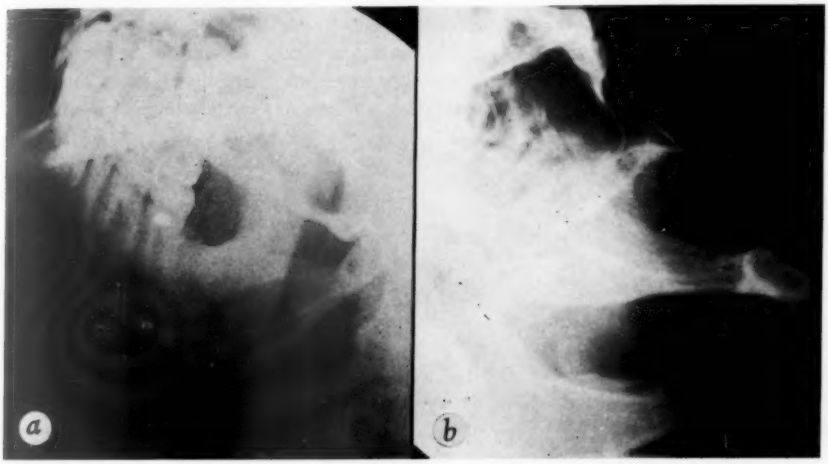

Fig. 2.—*a*, Cystlike defect in angle of mandible produced by metastatic hypernephroma. *b*, Metastatic adenocarcinoma from the breast.

Only one metastatic tumor, that secondary to the carcinoma of the prostate, was osteoblastic (Fig. 1). This lesion showed a loss of the normal trabecular pattern of the bone, with an indistinctness and haziness of outline. The central portion appeared to be more sclerotic, with diminishing density as the periphery was approached. Such production of bone is a frequent finding in osseous metastasis from the prostate.

Some of the osteolytic lesions simulated bone cysts in appearance (Fig. 2). Most of the cystic-appearing lesions were unilocular with regular, fairly well-defined outlines, while others were multilocular and showed scalloped, irregular outlines. A few of the larger tumors had produced extensive destruction of medullary and cortical bone. Despite this, only one pathologic fracture was demonstrable roentgenologically.

One of the lesions was indistinguishable roentgenologically from a dental periapical abscess and was so diagnosed after correlation with clinical symptoms. The appearance in two instances was suggestive of osteomyelitis of the jaws (Fig. 3). The involved zones had the classic worm-eaten appearance, with irregular osseous destruction surrounding islands of free dead bone.

In five cases, the roentgenologist believed that the osseous destruction was unequivocally on a malignant basis. Histologic evidence of metastasis was present in one mandible, even though the roentgenologic appearance was normal.

With two exceptions, one at the root apex of a maxillary tooth and one in the anterior mandible, none of the lesions were adequately demonstrated by the usual intraoral dental roentgenograms alone. Either posteroanterior or lateral views (or both) of the jaws were required to provide adequate evidence for determining the location and extent of the lesions.

Pathologic Aspects.—Many of the preserved surgical specimens consisted of small pieces of bone and tumor that had been excised for biopsy. In a few instances, the tumor and the surrounding bone had been subjected to wide local excision. Five of the specimens were resected portions of mandibles and adjacent structures. In most of the latter specimens, large zones of medullary

Fig. 3.—Metastatic squamous-cell carcinoma simulating osteomyelitis in appearance.

and cortical bone had been destroyed and the adjacent soft tissues had been invaded in an obviously malignant fashion. The lesions did not display any gross characteristics that could be of value in making a specific diagnosis.

From the histologic standpoint, most of the metastatic tumors bore a strong resemblance to the parent tumors, with recognizable squamous-cell or glandular elements. When it was possible to examine tissues from both the primary tumor and the metastatic lesion, they usually were identical. One outstanding exception was found when a highly anaplastic metastatic growth from a squamous-cell carcinoma of the lip presented the histologic appearance of sarcoma except for some central foci in which the basic carcinomatous tissue was identifiable.

Treatment.—Many of the patients in the present study had received attention elsewhere before coming to the clinic. In seven cases the condition

had been diagnosed as infection of dental origin. It had been treated accordingly by extraction of one or more teeth in four of these patients, by attempted incision for drainage in two, and by the use of various mouthwashes and excision of the lesion in the seventh. One patient was treated empirically for several days with antibiotics before biopsy disclosed the malignant nature of the disease process. One lesion was diagnosed and treated as a bone cyst, and one was diagnosed (without benefit of biopsy) as a primary malignant tumor and radiation was administered. Eight of the patients had not been treated before coming to the clinic.

Treatment at the clinic was preceded by biopsy in each case. Four patients had hemimandibulectomy combined with radical dissection of the neck, two had wide excision of the lesion, one had hemimandibulectomy followed by roentgen therapy, and one had local excision followed by roentgen therapy. Radiation in the form of radium or radon was used in three patients. Radiation of the lesion, castration, and administration of sex hormones were employed in the patient who had prostatic carcinoma and in one of the patients who had carcinoma of the breast.

Eight of these thirteen treated patients died of their malignant disease, although the lives of two of them were probably prolonged. There was inadequate follow-up of the remaining five patients, two of whom had been treated by hemimandibulectomy and two by radiation. It is reasonable to assume that, if the primary site of the tumor can be recognized and adequately treated in the very early stages, treatment of the metastatic lesion in the jaw can at least prolong life. In such instances, hemimandibulectomy and radiation, either singly or in combination, can be palliative and may effect a cure.

COMMENT

Metastatic carcinoma has been said to be the most common malignant tumor of bone.[13] Some authors[10, 21] have estimated that metastasis to bone occurs in approximately 20 to 50 per cent of carcinomas of the breast, kidney, prostate, lung, and possibly the thyroid. Metastasis to the jaws, however, appears to be infrequent; its apparent rarity is particularly noticeable when the small number of reported cases of metastasis to the jaws are compared with the thousands of reports of metastasis to other parts of the body.

It is possible that the jaws, like the bones of the limbs distal to the elbow and knee, seldom are hosts to metastatic deposits. On the other hand, this apparent rarity may be partially due to failure to recognize metastatic tumors in the jaws. Another factor to be considered is that the maxilla and mandible are seldom examined during necropsy.

It has been suggested that more metastatic lesions of the jaws would be detected if specific investigation of the jaws were included in roentgenographic surveys made for the purpose of locating metastatic growths.[16] Views of the skull may be included in such surveys, but in these views the jaws are usually so obscured that any lesions present might be overlooked. Of course, in their

early stages metastatic lesions of the jaw may not be detectable by roentgenographic means. Metastatic lesions of the jaw sometimes are not symptomatic and thus may be overlooked. This may be particularly true when the primary malignant tumor is far advanced and the patient has symptomatic metastatic deposits elsewhere.

In 1954, Castigliano and Rominger,[6] in a review of the literature from 1902 through 1953, were able to find a total of only 176 reported examples of metastasis to the jaws. Most were single case reports, but a few series were reported. They added seven new cases.

Since their review appeared, thirty-seven additional instances of metastasis to the jaws have been reported. These metastatic lesions came from primary tumors of the breast,[1-3, 14, 16-18] kidney,[11, 14, 17, 20] lung,[1, 12, 17-19] prostate,[4, 14, 15, 17] uterus,[7, 9, 17] sigmoid,[5] rectum,[15] lip,[14] and liver,[8] from melanomas of the skin,[1, 14] and from osteogenic sarcoma of the bones of the leg.[1]

This total of thirty-seven cases of metastasis to the jaw reported over a period of approximately four years, as compared with a total of only 183 cases reported in the preceding fifty-two years, apparently indicates an increased interest in the condition and a greater awareness that it can and does occur. Perhaps this heightened interest in and recognition of the condition by physicians and dentists may lead to the discovery that metastatic malignant tumors of the jaws are not as rare as the relative scarcity of cases heretofore reported would suggest.

SUMMARY AND CONCLUSIONS

A study of twenty cases of proved metastasis of tumors to the jaws has been presented. Only one of these lesions was observed in the maxilla. The metastatic tumors observed in the jaws originated in primary carcinomas of the kidney, breast, sigmoid, rectum, colon, prostate, lip, nose, tongue, and skin. Metastasis from sarcoma was not encountered.

The differential diagnosis is the outstanding problem in metastatic tumors of the jaws. This is particularly true when a solitary metastatic deposit is discovered without evidence of a primary source. Swelling was the only symptom that was common to all cases. Pain and neurologic symptoms were observed but were by no means characteristic. Extraoral as well as intraoral roentgenograms should be made. In all cases, because of the variability of the roentgenographic appearance, confirmation of metastasis should be made on the basis of histologic examination. More awareness of the possibility of metastatic tumors of the jaws should lead to their earlier histologic verification and thus forestall inappropriate therapeutic measures.

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AN UNORTHODOX INTRAOSSEOUS LESION OF THE MANDIBLE

Report of a Case

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IT HAS been fairly well substantiated that there should be no surgical interference in cases of fibrous dysplasia until after the patients have passed adolescence, since injudicious disturbance of these lesions during this period will cause them to proliferate more rapidly than if they are left unmolested. As illustrated by the following case, this is also true during a period of pregnancy.

CASE REPORT

A 19-year-old Negro woman came to the Albert Einstein Medical Center dental clinic in December, 1956, complaining of severe pain of one week's duration in the left mandible.

Five months earlier she had experienced a tender swelling of the left submandibular region. This was attributed to pericoronitis of the left third molars, and these teeth were extracted. The pain persisted, however, and the patient was referred to the x-ray department, where nothing of significance was found (Fig. 1). After two weeks of symptomatic treatment, the patient disappeared and was not seen again until the pain returned.

The patient was a well-developed, well-nourished young woman in her third month of pregnancy. Extraoral examination revealed a diffuse, tender swelling of the left mandible, measuring 3 by 2 cm., which was hard and fixed and had distended the inferior border (Fig. 2). No palpable lymph nodes were discernible.

Intraoral examination showed the left mylohyoid ridge and the inferior aspect of the ascending ramus to be enlarged and hard. The patient's temperature was 99.6° F. A tentative diagnosis of chronic osteomyelitis was entertained. Six hundred thousand units of procaine penicillin and 250 mg. tetracycline three times daily were prescribed. Routine complete blood count, urinalysis, serology, and lateral and anteroposterior jaw films were ordered.

The x-ray report indicated "rarefaction compatible with osteomyelitis rather than tumor" (Fig. 3).

After three weeks of continued antibiotic therapy, the lesion was unchanged and the pain persisted. The patient had a temperature of 98.6° F. Laboratory findings showed a blood sedimentation rate of 35 (elevation attributed to pregnancy) and an alkaline phosphatase level of 5.2 Bodansky units, indicating bone change. A review of previous roentgenograms in the light of further knowledge led to a new clinical diagnosis of monostotic fibrous dysplasia (Fig. 4).

Because the laboratory tests were not diagnostic, and since the possibility of tumefaction existed, an intraosseous biopsy was performed. Under block and infiltrative anesthesia, a mucoperiosteal flap was elevated and retracted. The outer cortical bony plate was lifted away,

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exposing the biopsy site. There was much hemorrhage. The interstices were found to be soft, granular, reddish in color, and encased in cortical bony crypts; they were not limited by membranes or capsules, and they continued from the body of the mandible up the ascending ramus. There seemed to be several nidi of origin. After the flap was returned and coapted,

Fig. 1.

Fig. 2.

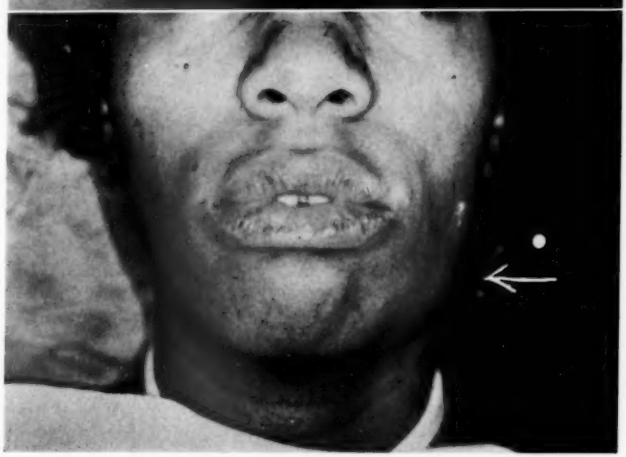

Fig. 1.—Roentgenogram taken on July 27, 1956, showing no evidence of pathologic change.
Fig. 2.—December, 1956. Note swelling of left mandible.

a tentative postoperative diagnosis of fibrous dysplasia was suggested and the material was sent for microscopic examination. The pathologist's report of Jan. 11, 1957, was as follows:

Microscopic: Sections of both the soft and the decalcified material show essentially the same pattern. It consists of trabeculae of well-established bone in

Fig. 3.

Fig. 3.—Roentgenogram taken on Jan. 1, 1957, showing rarefaction of left angle of mandible.

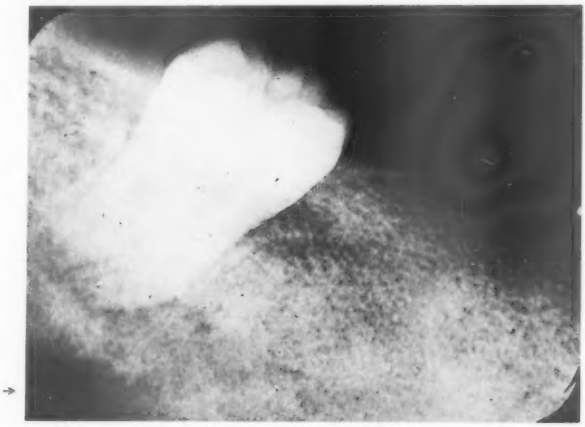

Fig. 4.

Fig. 4.—Note radiolucency 3 mm. inferior to apex of third molar (possible hamartoma) and areas which resemble characteristic "ground glass" and "orange peel," diagnostic of fibrous dysplasia.

the form of delicate spicules and some which are somewhat more dense. There is moderate fibrosis within the marrow spaces, producing a tissue that shows original fatty character with an increase in fibrous elements. Occasional foci of new bone formation are seen, but these are unrelated to areas of particular fibrotic activity and do not appear to be occurring as a metaplastic transformation of the fibrous background. Some spicules appear to be undergoing osteoclastic destruction. Though not typical, the possibility that we are dealing with sequestrum and involucrum must be entertained.

The postoperative course was entirely uneventful, and on the fifth day the sutures were removed.

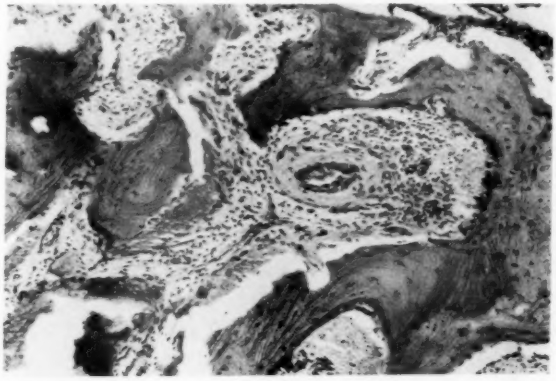

Fig. 5.—Photomicrograph showing areas of new bone and fibrous elements.

Since the surgical interference did not elicit the type of clinical response that one might expect is a chronic osteomyelitis, such as swelling, elevation of temperature, and possible collapse of periosteal flap, and since the pathologist's report did suggest an "increase in fibrous elements and occasional foci of new bone" (Fig. 5), it was our opinion that we were dealing with a fibrous dysplasia of the mandible which was increasing in size, due to the hormonal influence associated with pregnancy. More evidence was desired, however, and a bone survey was taken; this proved negative. The patient was referred for a complete hematologic work-up to determine either the presence of a sickle-cell or remote Cooley's anemia.

The patient had continually manifested a peripheral anemia in which hemoglobin varied from 8.4 to 10.7 grams, hematocrits from 32 to 34 per cent, and white blood cells from 8,400 to 17,700. Vitamin and iron therapy caused no dramatic improvement. A blood smear demonstrated a slight achromia, a moderate poikilocytosis, and a marked anisocytosis. Sickle-cell anemia was discounted, and megaloblastic anemia of pregnancy was ruled out.

During the ensuing months, the lesion grew larger until it occupied an area approximately 6 cm. in diameter. It was decided that a second biopsy might be more representative of the tumor, and on Feb. 23, 1957, the patient was operated on again. As before, burnt, granular, spongy bone was found; however, in an area adjacent to the inferior alveolar canal there were several crypts of bone which housed a granulation type of tissue different from that yet seen. The bone and granulation tissue were chiseled free en bloc and placed in 10 per cent formalin solution for histologic examination. Again, healing was uneventful, and the repair took less time than was anticipated. On the sixth postoperative day the sutures were removed. The pathologist's report follows:

> *Microscopic:* The essential tissue is a mixture of fibrous tissue infiltrated by quite characteristic plasma cells. These are almost sheetlike in distribution in some areas. The dispersal appears more neoplastic than inflammatory.

There are associated bone fragments and some infiltration by polymorphonuclear leukocytes.

In view of this appearance, the possibility of solitary plasmacytoma is strongly raised and should be followed up.

Diagnosis: Plasma cellular infiltrate suggestive of solitary myeloma.

A Bence Jones protein study of the urine proved negative.

Fig. 6.

Fig. 7.

Fig. 6.—Roentgenogram showing soft-tissue enlargement of left angle of mandible.

Fig. 7.—Photograph taken in December, 1957. Note greater distention of the inferior border of the mandible and greater soft-tissue reaction.

Total blood serum protein determinations were as follows: total protein, 63; albumin, 45.6 per cent; alpha$_1$, 5.7 per cent; alpha$_2$, 12 per cent; beta, 17.1 per cent; and gamma, 19.6 per cent. There was a slight increase in alpha$_2$ and beta and a decrease in albumin.

Serum electrophoretic study revealed a deviation from the norm, but this was not diagnostic of any particular entity. The electrophoretic curve, when compared with the curves obtained by Dr. Stanley Lane of Columbia University in his study of plasmacytoma of the mandible, proved nonidentical.

At this time, the most plausible treatment seemed to be irradiation. However, it was now mid-March; the lesion, though growing progressively, had not become rampant; and, since there was danger of x-radiation to the fetus, it was decided to keep the patient under observation until after her child was born. The patient gave birth to a normal female child on May 16, 1957.

Roentgenograms taken in June, 1957, showed even greater distention of the inferior border of the mandible and greater soft-tissue reaction (Figs. 6 and 7).

Fig. 8.—Roentgenogram showing rarefied areas filled with new bone.

In the absence of a definitive diagnosis, an exploratory operation involving the entire mass was performed on June 19, 1957. Sections were taken for study from varied areas of the disturbance. Complete enucleation or resection of the mandible at this time was contraindicated, since it could only have resulted in disfigurement of the patient on the basis of a problematic diagnosis.

Antibiotic therapy was maintained. The surgical site healed by first intention, but four weeks after the operation a small fluctuant area developed at the angle of the mandible. This was incised and drained, and the material was cultured. Streptococcus was identified as the causative organism. The incision soon healed with no immediate exacerbation. At no time was there an elevation of temperature.

The pathologist's report of the third biopsy, dated July 12, 1957, follows:

Microscopic: The decalcified sections show the marrow spaces completely filled with a loose, vascular, granulation tissue. Scattered through this granulation tissue are foci of cellular infiltration, many of which are similar to the plasma cellular foci seen in the previous biopsies. These foci are usually a mixture of plasmacytes, lymphocytes, and frequently polymorphonuclear leukocytes. There is seen also striking osteoblastic activity, with areas of new-bone formation.

Diagnosis: Chronic osteomyelitis.

Fig. 9.—Roentgenogram showing condyles completely free of lesion.

Because of the interesting histology and the strange clinical behavior of the lesion, there were several x-ray clinical pathologic conferences, with the result that some believed the lesion to represent chronic osteomyelitis and others believed it to be fibrous dysplasia.

The course followed for the next three months was one of watchful waiting, with the interesting observation that the lesion was regressing somewhat.

Roentgenograms taken in October, 1957, though still manifesting the deformity, showed the rarefied areas being almost completely filled with new bone (Fig. 8). However, on Oct. 31, 1957, the patient again returned, this time with marked trismus, pain on attempting to open the jaws and a strong deviation to one side. It was believed that (1) the growing mass had shortened the masseter muscle, restricting jaw movement, (2) a local inflammatory condition of the muscle had resulted from the trauma of mastication in a more confined oral space, or (3) the lesion had undergone malignant change and was destroying the condyle.

Complete laboratory examinations were made at this time, and all determinations were normal except for an elevated alkaline phosphatase of 8.8 Bodansky units.

The possibility of malignancy was strongly suggested by the persistent trismus and the elevation of alkaline phosphatase. The question of disarticulation and resection arose. Without a positive diagnosis, however, conservative watchful waiting was still the intelligent course to follow.

Fig. 10.

Fig. 11.

Fig. 10.—Sequestrum resorbed.
Fig. 11.—Contraction and filling of lesion.

On Nov. 20, 1957, one month after the onset of trismus, a fluctuant abscess localized at the angle of the jaw. This was incised and drained, the material was cultured, and sensitivity studies were made. The patient was then given 600,000 units of procaine penicillin in conjunction with 1 Gm. of tetracycline daily. At this time, an anteroposterior roentgenogram of the mandible revealed a small sequestrum with a sinus tract in the center of the filled lesion. Temporomandibular roentgenograms showed the condyles to be free of the lesion and consequently reduced the possibility of a malignant change (Fig. 9).

In spite of the persistent use of various types of antibiotics to which the organisms were sensitive in vitro, the area drained for approximately two months. On Jan. 15, 1958, chemotherapy was finally changed to novobiocin, 250 mg., and chloramphenicol, 250 mg.; all drainage ceased, the incised area closed, and the trismus disappeared. We can assume that it took this length of time for the small sequestrum to resorb (Figs. 10 and 11). The patient was symptom-free for the next nine months. However, on Oct. 15, 1958, a similar abscess localized at the same region and, after treatment with novobiocin and chloramphenicol, closed and healed. Roentgenograms revealed no further sequestrum formation.

Fig. 12.—The patient is now symptom-free, with no manifestation of disease. (Note that the left mandible is almost normal in contour.)

A follow-up study sixteen months after the last abscess found the patient symptom free with no manifestation of disease (Fig. 12). Of special interest is that fact that during this period the patient conceived and gave birth to a second child with no reactivation of the lesion.

DISCUSSION

I am of the opinion that this was a case of fibrous dysplasia with a coexisting chronic osteomyelitis, and I would like to postulate as follows:

A hamartoma was present in the mandible. This latent, congenital defect was disturbed by the trauma resulting from removal of a mandibular third molar. We can further deduce that the proliferation of this tissue was caused by the stimulus of the hormones associated with the pregnancy, for we are already acquainted with the fact that surgical interference in cases of fibrous dysplasia during the adolescent period has caused sudden expansive spurts of tissue growth with accompanying disfigurement.

With the postpartum changes in the hormonal level, the lesion regressed and filled with new bone. Since the bone in the expanding lesion was poorly

organized, it was susceptible to the development of ostemyelitis. Constant traumatic insult by the biopsy procedures activated that development.

SUMMARY

A 19-year-old female patient sought treatment of a swollen, painful jaw in July, 1956. Because of pericoronitis, the left maxillary and mandibular third molars were removed. The patient returned five months later with renewed pain and swelling and in a pregnant state. A review of former roentgenograms disclosed what could be considered a hamartoma at the inferior aspect of the left mandible. Because of the problematic diagnosis, three biopsy specimens were taken from different sites in the mandible. The jaw swelling increased continuously until the patient gave birth to a child in May, 1957. At this time, the swelling decreased and the rarefaction of bone filled.

Subsequent to this, the patient developed abscesses in the submaxillary region in November, 1957, and again in October, 1958. These were incised and drained, and they healed after treatment with a broad-spectrum antibiotic. Three years after the original complaint, the patient conceived and was delivered of a second child with no exacerbation of the orignial lesion. At no time during the second pregnancy was any oral surgical procedure performed.

It is my opinion that this was a case of fibrous dysplasia complicated by a chronic osteomyelitis.

CONCLUSION

A disfiguring rate of growth will most often be caused by any tampering with a lesion of fibrous dysplasia when the patient is in a state of hormonal activity, as during adolescence or pregnancy. (This was borne out in the present case by the fact that during the patient's second pregnancy, when there was no surgical intervention, there was no increased growth in the jaw.) Consequently, I believe that, difficult as it is, watchful surveillance without surgical interference is the treatment of choice in any undiagnosed bony jaw lesion which follows a benign course.

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6 OLD LANCASTER RD.

EXODONTIA

A SURVEY OF 3,874 ROUTINE FULL-MOUTH RADIOGRAPHS

I. A Study of Retained Roots and Teeth

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PROBLEMS associated with fractured and retained roots are frequently encountered in dental practice. Although there is general agreement among most dentists that, whenever possible, all fractured roots should be removed at the time of extraction, numerous surveys indicate that the average incidence of retained roots in patients presenting for dental examination is over 20 per cent.[3, 5, 7-9, 14, 21]

The high incidence of retained roots points up not only the need for full radiographic examination of all patients but also the frequency with which the dentist is faced with the necessity of surgical intervention to remove retained roots prior to prosthetic or restorative procedures. The decision to remove these roots must usually take into account several factors, such as the presence or absence of radiographic or clinical signs of infection, the extent of the surgical procedure required, the general condition of the patient, and the risk of a normal-appearing root becoming subsequently infected. Leading oral surgery textbooks[1, 4, 16] recommend that all root fragments discovered in routine radiographic examination should be removed. Mead[15, 16] states that all retained roots or root apices sooner or later become infected, even if the radiograph appears to be negative. This view is based on his impression that, upon surgical removal, the bone surrounding these roots is usually found to be "honeycombed." Stafne,[19] on the other hand, states that the majority of retained roots are not infected and that they may remain in the jaws indefinitely without causing any clinical symptoms. Stafne further believes that radiographic examination is a very reliable means of determining whether a retained root is or is not infected.

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The incidence of radiographic signs of infection associated with retained roots has been recorded in several studies. Swenson[21] noted an incidence of 9.6 per cent; Ennis and Berry,[9] in a more recent study, found an incidence of 5.9 per cent. Cheppe[3] noted the incidence of granulomas to be 7 per cent, but he adds that well over one-third of ninety-three roots examined showed "changes in the condition of the surrounding tissue" which he described as "thickening." It is apparent that the criteria employed in interpreting radiographic findings may account for variations in the incidence of infection ascribed to retained roots. This variation also raises the question of how reliable radiographs are in revealing the presence of infection surrounding a retained root.

Although the incidence of retained roots and radiographic changes associated with them has been investigated, a study of various factors which may influence the occurrence of these changes has not been reported previously. These factors include the length of time the root has been retained in the jaws, the age of the patient, the location and size of the retained root, and whether the root is completely enclosed in bone, lying partly in soft tissue, or even partially exposed to the oral cavity. It was the purpose of this study to investigate all but the first of these factors. (We could not include the length of time the roots were retained, since this information could not be determined from our records.) In addition, a survey of retained deciduous teeth and the roots of deciduous teeth was made.

MATERIALS AND METHODS

A series of 2,189 full-mouth radiographs from the Indiana University School of Dentistry and 1,685 full-mouth radiographs from the Dental School of the University of Oregon were included in this study. A series of radiographs was selected from the files, and no radiographs were eliminated unless a set was incomplete or faulty. The distribution of the two samples according to age groups and sex may be seen in Table I.

TABLE I. DISTRIBUTION OF FULL-MOUTH RADIOGRAPHS ACCORDING TO AGE GROUP AND SEX

AGE GROUPS	MALES		FEMALES		TOTALS	
	INDIANA	OREGON	INDIANA	OREGON	INDIANA	OREGON
11-20		89		186		275
21-30		179		284		463
18-30	259		404		663	
31-40	143	118	301	247	444	365
41-50	155	82	226	155	381	237
51-60	117	77	209	101	326	178
61 and over	178	112	197	55	375	167
Totals	852	667	1,337	1,043	2,189	1,685

In the Oregon group the occurrence of retained roots and the incidence of radiolucencies involving them was recorded. Records were also kept on the incidence of retained deciduous teeth and roots of deciduous teeth. The effect of anatomic location and age was noted. In the Indiana group, in addition to these factors, the relationship of radiolucency to root size, location within the

jaw, and the nature of the tissues surrounding the root (bone, soft tissue, or oral cavity exposure) was investigated. A series of 611 sets of occlusal radiographs of fully edentulous patients was included, and the incidence of retained roots and teeth in this group was tabulated.

INCIDENCE OF RETAINED ROOTS

The incidence of retained roots, according to age and location in the jaws, may be seen in Tables II and III. This sample includes both edentulous jaws and those in which a varied number of teeth still remain. It will be noted that,

TABLE II. INCIDENCE OF RETAINED ROOTS ACCORDING TO AGE

AGE GROUPS	INCIDENCE OF PATIENTS WITH RETAINED ROOTS	
	OREGON GROUP (PER CENT)	INDIANA GROUP (PER CENT)
18-20		10.7
21-30	7.6	
31-40	11.5	20.0
41-50	19.0	21.5
51-60	20.2	26.4
61 and over	37.8	29.4
Total incidence	13.9	20.0

while the incidence increases fairly consistently with age from approximately 10 per cent to as high as 38 per cent, the over-all incidence of retained roots was close to 20 per cent. These figures are in substantial agreement with other studies which were concerned predominantly with edentulous jaws.[3, 5, 7-10, 18, 20-22] It is interesting to note that the number of roots left in the jaws has not diminished appreciably over the past thirty years. The ratio of roots occurring in the maxilla to those in the mandible was approximately 2:1; the ratio of roots occurring in the posterior portion of the jaws to those in the anterior portion (cuspid and incisor areas) was approximately 6.5:1.

TABLE III. ANATOMIC LOCATION IN THE JAWS OF RETAINED ROOTS (DATA POOLED FROM INDIANA UNIVERSITY AND UNIVERSITY OF OREGON)

NUMBER OF ROOTS	MAXILLA	MANDIBLE
Posterior area	791	418
Anterior area	143	41
Totals	934	459

INCIDENCE OF RADIOLUCENCIES ASSOCIATED WITH RETAINED ROOTS

The presence of a small radiolucency around a retained root is not always easy to determine. The interpretation of "thickening" as representing infection is equally risky. The presence or absence of infection cannot be determined by means of a radiograph. For the purposes of this study, we considered any evidence of "thickening" or the presence of a narrow area of bone loss around a portion of the root as a radiolucency in the belief that these were the only consistent criteria which could be employed in tabulating data. The only

inference which these criteria permit one to make about the status of a retained root is that the likelihood of infection associated with such a root is greater than if no areas of bone loss or rarefaction whatever are visible on the radiograph. Data compiled in this fashion are more likely to be of some clinical value. The incidence of radiolucencies associated with retained roots of all types, according to age groups, is shown in Table IV.

TABLE IV. INCIDENCE OF RADIOLUCENCIES ASSOCIATED WITH RETAINED ROOTS (DATA COMPILED FROM INDIANA UNIVERSITY)

AGE GROUPS	NUMBER OF ROOTS WITH RADIOLUCENCY	PER CENT OF ROOTS WITH RADIOLUCENCY
18-30	114	72.2
31-40	98	56.0
41-50	93	52.5
51-60	118	55.9
61 and over	101	42.4
Totals	524	54.6

It may be noted that the incidence of radiolucencies was quite high, with over 50 per cent of the retained roots being involved. These figures are in marked contrast to those of other investigators,[3, 9, 21] which show an incidence of slightly below 10 per cent. Two factors may account for this difference. First, previous studies were performed exclusively in edentulous jaws, and presumably the vast majority of roots were not exposed to the oral cavity, a factor which has a marked influence on the incidence of radiolucencies. Second, previous authors, who did not indicate the criteria used to determine the presence of "infection" in the radiograph, may not have included cases of a borderline nature among the "positives."

The incidence of radiolucencies does not appear to vary greatly with age, with the exception of a somewhat higher (72.2 per cent) incidence in the age group under 30. As will be seen below, this increase is due mainly to the fact that in this group there is a great preponderance of retained roots exposed to the oral cavity in contrast to those enclosed within bone.

INCIDENCE OF RETAINED ROOTS AND TEETH IN EDENTULOUS JAWS

The incidence of residual roots and teeth was noted separately for edentulous jaws, while further data (see below) were pooled with findings in dentulous cases. The data on edentulous jaws are summarized in Table V. Each patient in this group had upper and lower occlusal radiographs. Ennis and Berry[9] and Storer[20] point out that periapical films in the lower anterior area, in addition to

TABLE V. INCIDENCE OF RETAINED ROOTS AND TEETH IN EDENTULOUS JAWS (DATA COMPILED FROM INDIANA UNIVERSITY)

Total number of fully edentulous patients with upper and lower occlusal radiographs:	611	
Patients with retained roots	145	(23.7%)
Patients with embedded teeth within bone	16	(2.6%)
Total number of patients with residual roots or teeth	161	(26.4%)

occlusal films, are desirable for the discovery of small root fragments in this area. Such films, however, were not available in the files of the patients in this study.

The incidence of retained roots and embedded teeth was 23.7 per cent and 2.6 per cent, respectively. These figures are essentially in agreement with the findings of previous authors in studies on edentulous jaws.

FACTORS AFFECTING THE OCCURRENCE OF RADIOLUCENCIES AROUND RETAINED ROOTS

The Location of the Root With Relation to Bone and Exposure to the Oral Cavity.—During the course of this investigation it became apparent that the two types of retained roots found within the jaws differ greatly in their susceptibility to infection as evidenced by radiographic study. The first type is the root fractured during extraction which, after the process of socket healing, becomes completely or almost completely enclosed within bone but, in any event, not exposed to the oral cavity. The other type of retained root is one which has resulted from the spontaneous fracture of the crown due to caries or other factors and which has remained exposed to the oral cavity and the oral fluids. When data relating to radiolucencies are separated into these two categories, a significant difference in incidence becomes apparent, as shown in Table VI.

TABLE VI. OCCURRENCE OF RADIOLUCENCIES WITH RETAINED ROOTS ACCORDING TO LOCATION WITHIN BONE OR EXPOSURE TO ORAL CAVITY (DATA COMPILED FROM INDIANA UNIVERSITY)

	ROOTS EXPOSED TO ORAL CAVITY	ROOTS WITHIN BONE OR SOFT TISSUES NOT EXPOSED TO ORAL CAVITY
Number of roots	540	419
Number of roots with radiolucency	438	86
Per cent of roots with radiolucency	81.1	20.5

Whereas roots exposed to the oral cavity exhibited associated radiolucencies in 81 per cent of cases, those contained mostly within bone were associated with radiolucency in only 20.5 per cent of cases. Viewed in this light, our data do not differ as significantly from those of previous investigators (20.5 per cent versus 7 to 10 per cent) as it appeared originally, since the latter considered primarily roots contained within bone in edentulous jaws.

It was recognized that in some instances it is not possible to discern radiographically whether a particular root is or is not exposed to the oral cavity. These cases were eliminated from the data in this section.

Size of Retained Root.—The possibility that the size of the root left behind at the time of extraction may have an effect on the development of radiolucencies was investigated. For the purposes of this study, roots were arbitrarily divided into two groups: retained roots judged to represent less than one-third of the original root size were classified as root tips, and roots representing one-third or more of the original were classified as larger root fragments. Retained roots exposed to the oral cavity were excluded from this study. The data from this

study are summarized in Table VII. It is evident that no significant difference in the incidence of radiolucencies exists when retained root tips are compared to larger root fragments.

TABLE VII. EFFECT OF ROOT SIZE ON OCCURRENCE OF RADIOLUCENCIES (DATA FROM INDIANA UNIVERSITY)

	ROOT TIPS	LARGER ROOT FRAGMENTS
Number of roots	256	161
Number of roots with radiolucency	53	38
Per cent of roots with radiolucency	20.7	23.6

Anatomic Location.—The methods and problems of extraction vary in different areas of the jaws. This variance has been used to explain the higher incidence of retained roots in the maxilla than in the mandible, as well as the great preponderance of retained roots in the posterior regions as compared to the anterior areas. A study was made to determine whether differences may exist in the susceptibility to radiolucencies around roots retained in different areas of the jaws. Retained roots exposed to the oral cavity were excluded from this study also. The area encompassing the cuspids and incisors was considered the anterior area. The results of this study are tabulated in Tables VIII and IX.

TABLE VIII. COMPARISON OF RADIOLUCENCIES IN MAXILLA AND MANDIBLE (DATA POOLED FROM INDIANA UNIVERSITY AND UNIVERSITY OF OREGON)

	MAXILLA	MANDIBLE
Number of roots	570	283
Number of roots with radiolucency	119	71
Per cent of roots with radiolucency	20.8	25.1

The incidence of radiolucencies in the mandible was 25.1 per cent, as compared to 20.8 per cent in the maxilla. This difference is not statistically significant. A significant difference became apparent, however, when radiolucencies in the posterior and anterior areas of the jaws were compared. While the incidence in the posterior area was 19.4 per cent, in the anterior region radiolucencies occurred in 40.3 per cent of the instances. This large difference seems difficult to explain, but it appeared to the same extent in the two separate studies conducted in Oregon and in Indiana.

TABLE IX. COMPARISON OF RADIOLUCENCIES IN POSTERIOR AND ANTERIOR AREAS OF JAWS (DATA POOLED FROM INDIANA UNIVERSITY AND UNIVERSITY OF OREGON)

	POSTERIOR AREAS	ANTERIOR AREAS
Number of roots	739	114
Number of roots with radiolucency	144	46
Per cent of roots with radiolucency	19.4	40.3

Retained Roots of Deciduous Teeth.—Faulty resorption of the roots of deciduous teeth, particularly molars, is not uncommon.[12, 13] In addition, thin, partially resorbed roots are often seen in deciduous teeth. As a result, fractured or retained deciduous root fragments frequently occur following extraction of deciduous teeth. Lindahl[13] states that there is no justification or need for removal of such apical tip ends, if the deciduous tooth is vital. Such retained roots may subsequently be resorbed, brought to the surface and shed as the permanent tooth erupts, or they may remain in the jaws. Diagnosis of a retained deciduous root can be made with assurance only when all permanent teeth in the area are present.

TABLE X. INCIDENCE OF RETAINED PRIMARY ROOTS* (DATA COMPILED FROM UNIVERSITY OF OREGON)

AGE GROUPS	NO. OF CASES WITH RETAINED ROOTS	AREA OF RETAINED ROOTS			
		LOWER POSTERIOR	LOWER ANTERIOR	UPPER POSTERIOR	UPPER ANTERIOR
13-20	6	6	–	–	1
21-30	5	6	1	–	2
31-40	4	5	1	–	1
41-50	3	2	–	1	–
51 and over	3	2	–	1	–
Totals	21	21	2	2	4

*Based on 1,665 full-mouth radiographs.

A survey was made of the incidence of retained deciduous roots (Table X). It may be noted that, while retained deciduous roots can be observed in all age groups, the incidence is quite low—1.2 per cent. The great majority of these occur in the lower posterior area. Judging from the considerably higher incidence of retained roots of permanent teeth, the data from this study seem to indicate that the majority of deciduous roots remaining in the jaws following extraction are either resorbed or exfoliated.

TABLE XI. INCIDENCE OF RETAINED DECIDUOUS TEETH (DATA FROM UNIVERSITY OF OREGON)

Number of radiographs in study		1,710
Number of cases of retained deciduous teeth		27
Incidence of retained deciduous teeth		1.6%
Types of retained teeth:		
Upper cuspids	23	
Lower molars	7	
Upper molars	6	
Other	5	

Retained Deciduous Teeth.—Deciduous teeth may be retained whenever succeeding permanent teeth are congenitally missing, impacted, or unable to erupt for other reasons. In a study of 150 retained deciduous teeth, Austin and Stafne[2] found that the majority were found to be maxillary cuspids and lower second molars. Sixty-nine per cent of these retained teeth were associated with the congenital absence of permanent teeth, and 28 per cent were associated with impacted teeth. The results of our study are tabulated in Table XI. The

ratio of patients with retained deciduous teeth to those in the total sample was 1:63. Maxillary cuspids constituted more than half (56 per cent) of the retained teeth, with lower and upper molars next in frequency.

SUMMARY

A comprehensive study of 3,874 routine full-mouth radiographs yielded the following findings concerning retained roots and teeth:

1. The incidence of retained roots discovered in routine full-mouth radiographs of all types of patients was close to 20 per cent. Twice as many roots are retained in the maxilla as in the mandible, and over six times as many are retained in posterior areas as in anterior areas.

2. The incidence of retained roots in edentulous jaws was close to 24 per cent, and the incidence of retained and embedded teeth was 2.6 per cent.

3. The over-all incidence of radiolucencies associated with retained roots was over 50 per cent.

4. Of these retained roots, those exposed to the oral cavity were involved with radiolucent areas in 81 per cent of the cases, while roots lying beneath the surface or completely encased in bone had radiolucent areas around them in 20 per cent of the cases.

5. The size of the retained root had no influence on the incidence of associated radiolucent areas.

6. There was no difference in the numbers of radiolucencies between roots found in the maxilla and those found in the mandible, but a markedly higher incidence of involvement was noted in anterior areas as compared to posterior areas.

7. The incidence of retained roots of deciduous teeth which remain in the jaws is extremely small (1.2 per cent).

8. Retention of deciduous teeth occurred in one out of every sixty-three patients. The most frequently retained deciduous tooth was the maxillary cuspid.

The significance of these findings is discussed, and the need for comprehensive radiographic examination of all patients is emphasized.

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HISTOLOGIC ASSAY OF HEALING FOLLOWING ULTRASONIC CURETTAGE VERSUS HAND-INSTRUMENT CURETTAGE

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In a previous report it was concluded that ultrasonic curettage constituted an excellent method of débridement of the sulcular wall of the periodontal pocket. The purpose of this report is to illustrate findings concerning the relative effectiveness of the ultrasonic and hand-instrument procedures.

MATERIAL AND METHODS

Fifteen operative fields each of ultrasonic curettage and of hand-instrument curettage were studied. The procedure consisted of prescaling, for each method, two similarly involved selected adjacent sites, followed by curettage of one area one week later. An adjacent untreated area served as a control. The anterior portion of the dentition was the operative site, but only the marginal area was investigated. This allowed for ease of approach and a certain uniformity of operative management by both methods. The cases selected for the experiment were those usually indicated for the curettage procedure; the pocket depth ranged up to 4 mm. Since the control section and both surgical operations were performed in the same patient, healing factors were uniform. The hand instruments utilized were a small scaler and the Goldman-Fox curette No. 2. For the ultrasonic method, a blunt or small scaler was used for the débridement, whereas a larger straight tip was used for scaling. Biopsies were performed fourteen to sixteen days postoperatively.

The specimens were fixed in formalin, and histologic preparations were made; hematoxylin and eosin stain was used. The criteria for healing were the character of the sulcular epithelium and the condition of the gingival corium.

FINDINGS

Only the curettage findings are reported here.

Hand-Instrument Procedure.—Histologic examination of the fifteen specimens disclosed a distinct healing process, in contrast to the control sections.

From the Department of Stomatology, Boston University School of Medicine.

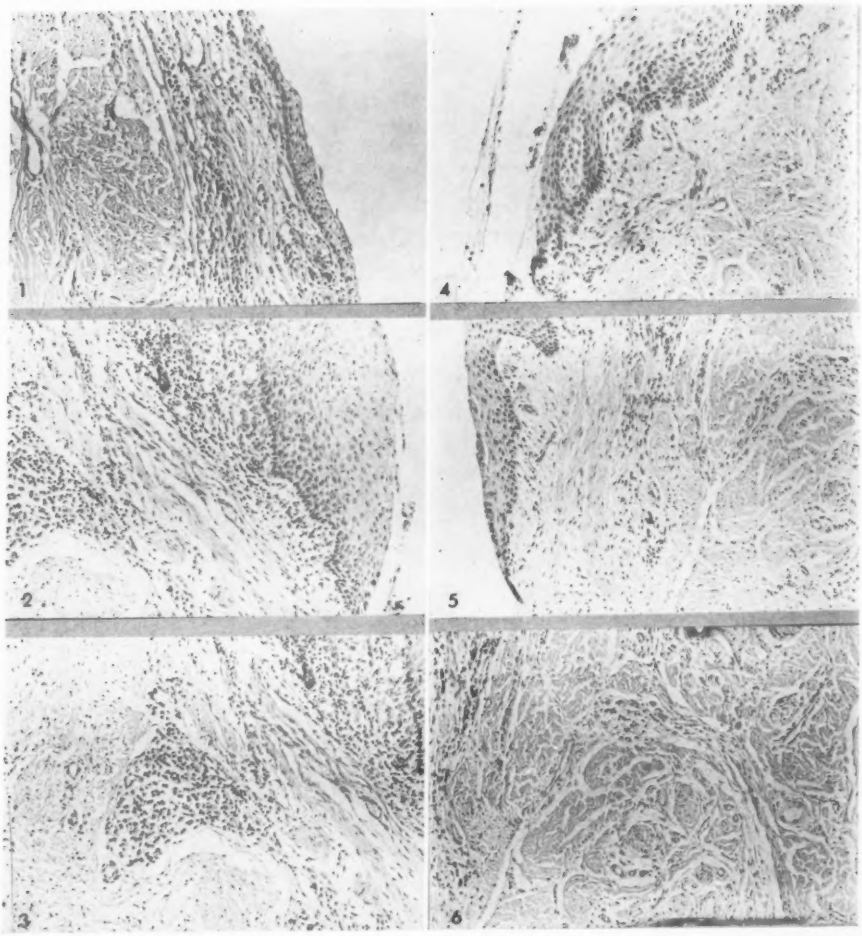

Fig. 1.—Photomicrograph of the sulcular epithelium and adjacent gingival corium in a section treated by hand-instrument curettage. The epithelization is complete. There is a scattering of inflammatory cells in the subsulcular area. Deeper in the corium the gingiva is composed of fibrous connective tissue.

Fig. 2.—Photomicrograph of the sulcular epithelium and adjacent gingival corium in a section treated by hand-instrument curettage. Note the thickness of the epithelium and the presence of some inflammatory cells in it. There is a marked subjacent inflammatory infiltrate as well as a focus of inflammatory cells deeper in the gingiva.

Fig. 3.—Photomicrograph of the gingival corium seen in Fig. 2. Note the accumulation of inflammatory cells.

Fig. 4.—Photomicrograph of the sulcular epithelium and adjacent gingival corium in a section treated by ultrasonic curettage. The sulcular epithelium is intact, and subjacent to it there is no accumulation of inflammatory cells. The connective tissue of the gingiva is relatively free of inflammatory cell infiltrate.

Fig. 5.—Photomicrograph of the sulcular epithelium and adjacent gingival corium. Note the intact sulcular epithelium and the absence of any focal accumulation of inflammatory cells.

Fig. 6.—Photomicrograph of the body of the gingival corium seen in Fig. 5. Note the fibrous connective tissue and the slight sprinkling of inflammatory cells.

In six cases the sulcular epithelium consisted of a thickness of several cells and was intact, with no rete pegs present; in three cases the sulcular epithelium was quite thick. In another three cases, there was distinct proliferation of the sulcular epithelium into the gingival corium as a result of an inflammatory process, and the remaining three cases exhibited a more advanced pseudoepitheliomatous hyperplasia. In the nine specimens with complete epithelization, a repair process was seen in the corium, with production of collagen. In the remaining specimens a great deal of edema and inflammation was observed. In all the specimens there was still a sprinkling of inflammatory cells throughout, with a fairly marked infiltration in the subsulcular area. Perivascular accumulations were common; the cells consisted chiefly of lymphocytes and plasma cells.

Ultrasonic Instrumentation.—Comparison of the treated areas versus the control areas disclosed three distinct changes. First, in all cases except one, the sulcular epithelium was intact and, for the most part, consisted of several cell thicknesses; in four instances the sulcular lining was quite thick. Second, the gingival corium was quite free of inflammatory cells, with a mild sprinkling being observed; in three instances the tissue was relatively free. In ten specimens there was no marked subsulcular inflammatory infiltrate. Third, the gingival corium was composed of a moderately dense fibrous connective tissue.

Comparison of Sections of Ultrasonic and Hand-Instrument Curettage.—A composite study showed the essential differences between the specimens of these two groups to be in the character of the sulcular epithelium, the presence of a marked accumulation of a subsulcular inflammatory infiltrate, the perivascular grouping of lymphocytes and plasma cells in the corium, and the composition of the corium with respect to the connective tissue element. In the ultrasonic curettage group, the sulcular epithelium was free of inflammatory infiltrate and showed but little rete peg proliferation, and most of the specimens revealed only a sprinkling of inflammatory cells through the connective tissue. On the other hand, the hand-instrument curettage specimens disclosed many more inflammatory cells in the corium and in the subsulcular area. The sulcular epithelium was ulcerated and proliferating in three cases, and the sulcular epithelium in three other cases was undergoing a milder form of the same process.

CONCLUSIONS

On the basis of histologic evidence from fifteen operative sites subjected to prescaling and débridement by hand instrument, as compared to fifteen sites treated by ultrasonic instrumentation, it was disclosed that there was a marked diminution of inflammatory infiltrate in the gingival corium of areas treated with ultrasonic instruments. Complete epithelization covering the wound took place in fourteen out of fifteen cases of ultrasonic débridement, whereas this complete epithelization occurred in nine cases in which hand instruments had been used for the same procedure. An essential difference lay in the presence of a subsulcular inflammatory infiltrate in the cases treated with hand instruments.

On the basis of the above findings, healing following ultrasonic curettage can be considered more satisfactory than that which follows hand-instrument curettage.

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ORAL MEDICINE

IMMUNOLOGIC THROMBOCYTOPENIC PURPURA

Report of a Case

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PURPURA is a condition characterized clinically by petechiae or ecchymosis in the skin as well as by hemorrhage from mucous membranes and bleeding into various tissues. It is often associated with thrombocytopenia but may also be involved with increased capillary fragility, simultaneously or independently.[7]

If thrombocytopenia occurs, we can assume that platelet production is decreased or that platelets produced in normal numbers are being destroyed or removed from the circulation at a higher rate than normal. Immunologic thrombocytopenia indicates excessive platelet destruction with no significant reduction in platelet formation. It is believed to be a direct action on the platelets produced by a circulating antiplatelet agglutinin.[5] For example, in the case of thrombocytopenia produced by quinidine, administration of a test dose of the drug after the platelet count had returned to normal produced a precipitous drop in platelets from 325,000 per cubic centimeter to 25,000 per cubic centimeter in two hours. Even if all platelet production had been completely paralyzed by the quinidine, it would have taken approximately three days to reduce the level of circulating platelets to such a low figure. Other studies on so-called "idiopathic" thrombocytopenic purpura often showed a powerful antiplatelet agglutinin to be absorbed by the platelets.[10] When normal platelets were transfused to the patient, they rapidly disappeared from his blood, and administration of his plasma to a normal recipient caused a striking decrease of the recipient's circulating platelets.[9] Antibodies have been demonstrated in a patient's blood for as long as six months following discontinuance of quinidine therapy, even though the thrombocytopenia had subsided completely.[12] It is also concluded that altered morphology of the megakaryocytes (probably platelet producers) in the bone marrow is caused by the same lysin or agglutinin which affects the circulating platelets.[3]

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Agents to which this immunologic thrombocytopenic state can be attributed are Sedormid, a sedative no longer in vogue; quinidine, a drug often used in the treatment of auricular fibrillation and other cardiac arrhythmias; and quinine.

Athrombocytopenic purpura due to chlorothiazide (Diuril, a very popular nonmercurial diuretic) has been reported.[6] An immunologic pathogenesis acting on the capillary endothelium qualitatively is suggested.[1] Quinine, sulfapyridine, and digitoxin are among the drugs known to cause athrombocytopenic purpura, although they are more often associated with the thrombocytopenic variety. Allergic purpura due to a variety of foods, infections, and drugs has been reported with good circumstantial evidence. The drug list includes arsenobenzol compounds, sulfonamides, iodides, chrysarobin (employed locally in ringworm, psoriasis, and eczema), insulin, and menthol.[2]

Oral Signs.—Ecchymosis of the oral mucous membranes and bleeding from the gingival tissues around the teeth are almost uniformly reported in cases of thrombocytopenic purpura, with a lower incidence in the athrombocytopenic form. The rapid action of the above-stated mechanism will cause sudden onset of bleeding symptoms. In the case reported here the only symptom when the patient presented for dental treatment was profuse gingival bleeding. Attempts to treat the condition locally without investigating the cause resulted in failure.

CASE REPORT

A 61-year-old white male storekeeper was admitted to Montefiore Hospital with a chief complaint of bleeding from the mouth. The patient had been well until four hours prior to admission, at which time he had noticed blood in his mouth after eating a raw apple. His dentist packed the more obvious bleeding gingival crevices with Oxycel, but clotting failed to occur.

There was no history of liver or gall bladder disease, jaundice, hematemesis, hematuria, hemoptysis, rectal bleeding, bleeding from the ears, conjunctival hemorrhage, vitamin C deficiency, recent x-ray exposure, splenomegaly, bleeding disorders, or hemophilia. The patient had been under Serpasil treatment for hypertension until recently, when he was placed on Tuinal and Raudixin. Three months prior to admission he was given a one-week course of quinidine for paroxysmal atrial fibrillation. He had not taken any more quinidine until two hours before the mouth-bleeding episode, when he took one tablet for relief of palpitations.

Pertinent physical findings were as follows: blood pressure 160/94; temperature, 99° F.; pulse rate, 100. The skin tone was good, but ecchymosis and petechiae had developed while the patient was in the waiting room. Dermographia was easily elicited. All other findings were negative.

Oral examination showed profuse bleeding from the gingival crevices around all of the teeth and from bullous hemangioma-like swellings on the buccal and labial mucosae and on the floor of the mouth; bleeding was particularly profuse in the molar and premolar regions.

Laboratory examination showed a hematocrit of 49; a white blood count of 9,800, with 84 polymorphonuclear leukocytes, 14 lymphocytes, 1 eosinophil, and 1 monocyte; and a platelet count of 10,000 (normal, 250,000). There was 2 plus stainable iron in the sternal bone marrow with erythroid, myeloid, and megakaryocytic series of normal numbers and maturity, which indicated a hemolytic processus. Prothrombin time was 11.6 seconds. The urine showed 0 to 2 red blood cells and 1 to 3 white blood cells with 1 plus albumin. Blood urea nitrogen was 24.5 mg. per cent. Total protein was 7.2 Gm. (albumin, 4.2; globulin, 3.01).

The patient continued to bleed from the mouth for twelve hours following his admission to the hospital. Repeated packing failed to produce clotting, and the blood finally clotted spontaneously. By the following day all oral bleeding had stopped, and two days later there were no oral petechiae, bullae, or ecchymoses. The only treatment was discontinuation of the quinidine therapy. The following record shows the return of the platelets:

Oct. 28, 1958— 10,000
Oct. 29, 1958— 20,000
Oct. 30, 1958— 40,000
Oct. 31, 1958— 30,000
Nov. 3, 1958—200,000

The patient was discharged one week after the platelet count had returned to normal.

DISCUSSION

From the effects of varying the initial concentration of each component of the complex on the amount of complement fixed, from the kinetic aspects of the sequential reactions, and from other chemical and physical properties of the various components involved, Shulman[11] deduced a steric and kinetic model for the sequence and mechanism of reactions leading to (1) formation of a complex from an antibody, a haptene (quinidine), and a cell membrane (platelets) and (2) fixation of complement by the complex. The results of this study were consistent with the possibilities that the protein moiety of a haptenic antigen involved in the development of an antibody which attaches to a cell is not necessarily a component of the cell and that the cell reacts with the antibody by virtue of having a surface that is favorable for nonspecific adsorption of certain haptene-antibody complexes. Shulman's conclusion from in vivo studies contradicted the direct destruction of the platelets by the antibody. The minimal amount of antibody which attached to the platelets appeared to increase their susceptibility to the usual mechanisms of sequestration. Megakaryocytes and blood vessels did not appear to be affected by the antibody which causes quinidine purpura, and hemorrhagic manifestations of the disease appeared to be consequent to changes in the platelets alone.

Attempts to apply this single immunologic mechanism to all cases of idiopathic thrombocytopenic purpura that are characterized by a variable clinical course with spontaneous remissions and relapses, an inconsistent response to splenectomy or to the administration of adrenosteroids and adrenocorticotropic hormone (ACTH), and discrepancies between degree of hemorrhagic manifestations and level of circulating platelets and between the severity of the disease and the presence in vitro of platelet agglutinin should be avoided. The exact mechanisms of megakaryocytes, platelets, capillaries, spleen, antibodies, and hormones and their interactions in the pathogenesis of this disease have not yet been fully explained.

CONCLUSIONS

Chemotherapy is constantly increasing and changing with the introduction of new drugs and new therapeutic regimes for existing drugs. Although no drug is without possible side reactions, certain ones are more prone to create

hematologic problems. Disturbances in the clotting mechanism usually create serious problems in the oral cavity, even in the absence of dental procedures. Local measures to stop the bleeding are essential and often lifesaving, but they are transient at best if the underlying mechanism of disturbance is not determined and corrected. When confronted by symptoms of a bleeding disorder, the dentist should endeavor to obtain a complete record of all drugs taken, including nonprescribed remedies, and he should be constantly aware of their possible role in rapidly producing hemorrhagic symptoms in the oral cavity. Several such drugs and groups of drugs are mentioned in this report, and it seems safe to assume that more will be added.

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123 EAST 37TH ST.

THE MYOFASCIAL TRIGGER MECHANISM IN TEMPOROMANDIBULAR JOINT AND ALLIED DISTURBANCES

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INTRODUCTION

It is always best to start a discussion with a definition of terms. Therefore, I shall explain briefly some of the terms used to describe various aspects of pain of myofascial origin.

Myofascial pain is the term applied to those pain syndromes that originate in myofascial structures.

A *myofascial trigger area* is a small, circumscribed, very hypersensitive area in myofascial tissues from which impulses arise to bombard the central nervous system and produce referred pain. This area exhibits deep hyperalgesia, fasciculation, and referred pain. It should be emphasized that the myofascial trigger area is only a physical sign, not a symptom, and the patient is ordinarily unaware of its presence.

The *zone of reference* is the region in which pain, hyperalgesia, muscle spasm, and certain autonomic concomitants are produced by a myofascial trigger area.

MYOFASCIAL PAIN MECHANISM

The mechanism of myofascial pain involves some sort of pathophysiologic disorder, possibly a feed-back neuron circuit, which produces a self-perpetuating pain cycle. Evidently, fixed anatomic circuits are involved, for the zone of reference is the same for all patients, making it possible to locate the myofascial trigger areas from the position of the zone of reference. Patients can localize referred pain with surprising accuracy.

Activating Stimuli.—Myofascial trigger areas may be activated by such stimuli as motion that stretches the structure, pressure, needling, intense heat or cold, prolonged cooling, and drafts. Obviously, activation of these trigger areas is a problem in dentistry, for dental treatments stretch the mandibular musculature and dentists frequently use local anesthetics which may cause activation.

Manifestations.—The action of the myofascial trigger mechanism covers a broad area, of which the face and head[1, 2] are only a part. For example, as

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Travell[3] has shown, the myofascial trigger mechanism can be demonstrated in varied visceral and somatic pain syndromes, tension headaches, painful torticollis, calcific bursitis, myocardial infarction, effort angina, musculoskeletal chest pain, low back pain, sciatica, postoperative and traumatic pain syndromes, pain of hysteria, and a syndrome of dizziness and headache.

Pain caused by hysteria must not be removed merely by blocking the myofascial trigger mechanism, for this pain is the patient's only means of resolving his inner conflicts and its removal will lead to disintegration of the ego. Psychotherapy is essential in these cases, and the psychiatrist alone can tell when it is safe to remove any physical cause of the pain.

Precipitating Factors.—According to Travell,[3] the precipitating causes of myofascial trigger areas include (1) sudden trauma to musculoskeletal structures; (2) unusual or excessive exercise; (3) chilling of the body; (4) immobilization; (5) an acute visceral lesion, as in myocardial infarction or appendicitis, with localized reflex spasm of the skeletal musculature; (6) acute arterial closure in the extremities, as in popliteal thrombosis; (7) rupture of an intervertebral disc with nerve-root pressure; and (8) acute emotional stress.

It is obvious that the first two precipitating factors cited by Travell can develop during the course of dental treatment. In addition, the dentist frequently treats patients in whom acute emotional stress is evident.

Predisposing Factors.—Travell[3] lists the following predisposing conditions: (1) chronic muscular strain, produced by repetitive movement frequently performed over a long period of time; (2) general fatigue; (3) acute infectious illness, such as infectious mononucleosis, acute hepatitis, or an acute upper respiratory infection (postinfectious myalgias); (4) a chronic focus of infection; (5) nutritional deficiencies; (6) a progressive lesion of the nervous system; (7) nervous tension; (8) syndromes of the menopause and male climacteric; and (9) hypometabolism with creatinuria.

"Chronic muscular strain, produced by repetitive movement frequently performed over a long period of time" is an excellent description of the grinding and clenching of teeth frequently observed in dental patients. Dentists also see many patients in whom nutritional deficiencies, nervous tension, and menopausal and male climacteric symptoms are apparent.

Treatment.—The myofascial trigger mechanism must be completely blocked. Otherwise, the area may become latent, only to be reactivated at some future time. When the involved muscle is accessible, I prefer to spray ethyl chloride in long, sweeping strokes, holding the spray bottle just far enough from the skin to prevent whitening. The myofascial trigger area may also be treated by the injection of a local anesthetic (without a vasoconstrictor) into the area. I prefer ethyl chloride because injections further upset persons who are emotionally disturbed, as so many of these patients are.

TEMPOROMANDIBULAR DISTURBANCES

In an earlier publication,[4] I offered the following classification of temporomandibular disturbances in which myofascial pain may be involved:

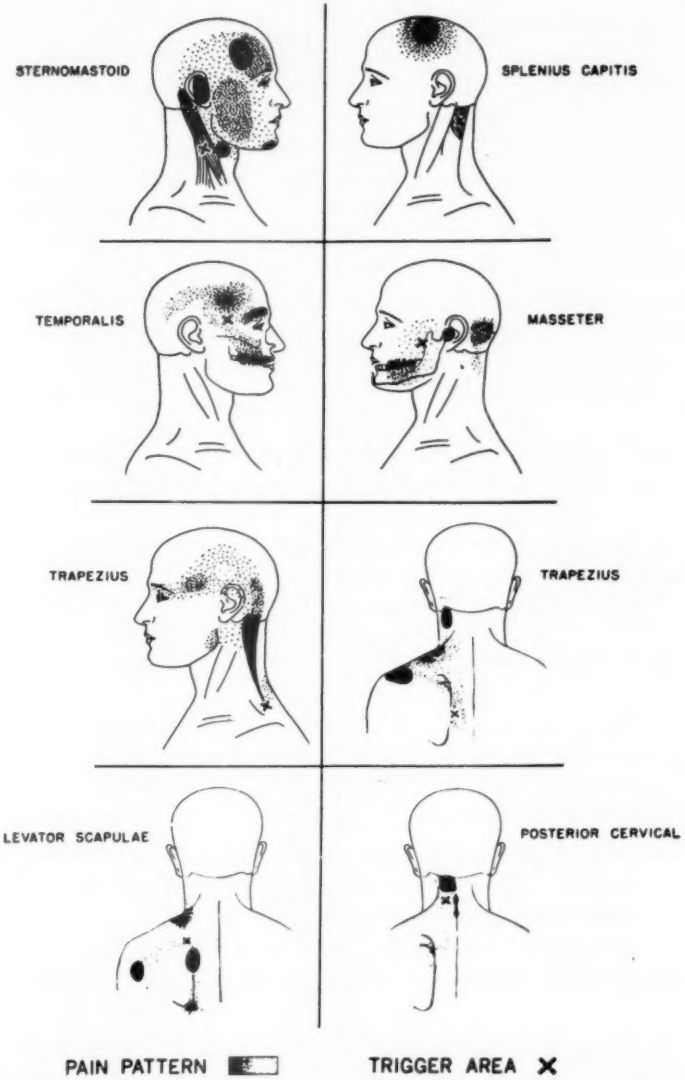

Fig. 1.—The pain reference patterns of myofascial triggers most commonly found in the skeletal muscles of the head and neck. The solid black areas represent the so-called "essential" zones in which pain appeared in 100 per cent of the patients, and the stippled areas represent the so-called "spill-over" zones in which pain appeared in less than 100 per cent of the patients. The heaviness of the stippling indicates the relative frequency of occurrence. (From Travell and Rinzler: Postgrad. Med. **11**: 427, 1952.)

1. *Traumatic disorders:* The symptoms are pain, swelling, limitation of motion, and muscle spasm. The patient's history and clinical and roentgenographic examinations will establish the diagnosis.

2. *Neoplastic conditions:* The symptoms, which include pain, may simulate other disorders. Neoplastic disturbances are relatively rare and are usually the result of metastasis from a primary tumor elsewhere in the body. Roentgenographic examination will establish the diagnosis.

3. *Infectious processes:* The symptoms are pain, swelling, limitation of motion, and occasionally systemic involvement. These conditions also are relatively rare and usually represent an extension from an infectious process in the neighboring structures.

4. *Arthritis:* This includes both degenerative joint disease (osteoarthritis) and rheumatoid arthritis. The symptoms are pain, stiffness, and joint sounds. In the early stages it is impossible to make a differential diagnosis on the basis of clinical or roentgenographic examination.

In 1959 I suggested a classification of pain for diagnostic purposes. This classification, which is based on location and on whether the pain is primary or referred, follows:

1. *Dental pain:* Pain in and about the teeth is usually caused by a pathologic condition of the hard and soft tissues of the teeth and periodontal tissues. In rare cases, however, the pain may be of psychogenic origin. (In a case referred to me, it was finally discovered that whenever the patient had emotional difficulties her "teeth would ache.")

2. *Mouth and throat pain:* First, the possibility of local pathologic factors must be ruled out. Trigger areas in the pterygoid muscles can refer pain to the throat, and trigger areas in the digastric and geniohyoid muscles can refer pain to the tongue.

3. *Face and head pain:* Here, also, local pathologic factors must be ruled out first. Referred pain can be due to zones of reference and also to dental pathologic conditions.

4. *Temporomandibular joint pain:* This pain may be caused by local pathologic changes, or it may be referred from a myofascial trigger area.

5. *Ear pain:* Possible local pathologic factors must be ruled out first. As Travell and Rinzler[5] have indicated (Fig. 1), the ear is frequently the site of referred pain.

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CLINICAL LABORATORY STUDIES ON A NEW TOPICAL CORTICOSTEROID—TRIAMCINOLONE ACETONIDE

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(With the assistance of Ana Tiburcio)

TRIAMCINOLONE ACETONIDE (Kenalog), a new corticosteroid, has been introduced into dental therapeutics for the treatment of acute and chronic lesions of the oral mucous membranes, such as recurrent ulcerative stomatitis, erosive lichen planus, desquamative stomatitis, etc.[1, 2] Triamcinolone acetonide has been incorporated in an adhesive vehicle which maintains high concentrations of the active agent at the site of these lesions, thereby permitting the use of minimal amounts of the active ingredient. In this way the amount of corticosteroid made available for systemic activity is considerably reduced. Nevertheless, small though this dosage may be, one cannot escape the possibility of an ultimate systemic action of triamcinolone acetonide, either through local absorption or through absorption in the remainder of the gastrointestinal tract following ingestion.

It was the purpose of this investigation to determine, if possible, the presence or absence of systemic effects of triamcinolone acetonide exclusively and solely on the basis of results obtained through blood and urine examinations of patients receiving triamcinolone acetonide during therapy for chronic lesions of the oral mucous membranes.

Triamcinolone acetonide is a new synthetic corticosteroid (a derivative of triamcinolone) which has been found to be particularly active upon topical application, although it is also fully active when administered systemically.

The results of an initial five-day cotton-pellet test[3] in adrenalectomized rats indicate that triamcinolone acetonide possesses anti-inflammatory activity equal to about twenty to thirty-five times that of hydrocortisone acetate, ten times the activity of prednisolone and ten times the activity of triamcinolone alcohol as an anti-inflammatory agent in animals.

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This study was supported in part by a grant-in-aid from E. R. Squibb & Sons, The Squibb Institute for Medical Research, New Brunswick, New Jersey. Triamcinolone acetonide in an adhesive base (Orabase) was supplied through the courtesy of The Squibb Institute for Medical Research.

Triamcinolone acetonide has been compared to cortisone acetate, hydrocortisone acetate, and triamcinolone alcohol in glucocorticoid activity by the rat liver glycogen assay.[3] In this test, it showed a potency over ninety times that of cortisone, twenty times that of hydrocortisone acetate, and more than nine times that of triamcinolone alcohol.

Thus far, triamcinolone acetonide has exhibited no sodium-retaining activity in animal experiments[3]; rather, it has produced an excretion of sodium.

Triamcinolone acetonide has been used topically almost exclusively in man. The compound has been administered systemically to human subjects primarily to supply pharmacologic data.

Triamcinolone acetonide was administered[3] orally to five patients with rheumatoid arthritis in doses ranging from 1 to 10 mg. for periods of one week to two months. All the patients had previously been satisfactorily maintained relatively free from signs and symptoms of the disease with prednisone in doses of 7.5 to 15 mg. per day. In two patients triamcinolone acetonide was as effective as prednisone in controlling signs and symptoms of the disease (in one patient at a dose level of less than 1 mg. per day), while in the other three patients triamcinolone acetonide was less effective. One patient experienced drowsiness, anorexia, and weight loss (4 to 5 pounds) over a period of one month, but no other undesirable or untoward effects of the administration of triamcinolone acetonide were reported. No clinical evidence of significant electrolyte disturbance was noted.

Triamcinolone acetonide was administered[3] to four children (aged 5½ to 9 years) in relatively massive single oral doses (30 to 50 mg.). Suppression of 17-ketosteroid excretion (as measured in twenty-four-hour urine samples), as well as suppression of endogenous corticoid production (as measured by both the blue tetrazolium and Porter-Silber reactions) was observed. Maximum suppression of endogenous corticoid production occurred within twelve hours of administration, and this suppression persisted for as long as thirty-six hours.

Studies concerned with the therapeutic effectiveness of this compound have been reported separately.[1, 2]

METHODS

This study involved eleven adult patients, two men and nine women, aged 23 to 68 years. All patients were ambulatory and in essentially good health, except for their oral lesions, at the time of therapy. The oral lesions under treatment included acute periodontitis in one patient, denture stomatitis in one patient, recurrent ulcerative stomatitis in three patients, idiopathic chronic palatal inflammation in one patient, idiopathic burning of the tongue in one patient, erosive lichen planus in three patients, and desquamative gingivitis in one patient.

Prior to therapy, patients were subjected to a battery of blood and urine examinations (in the fasting state), including in each instance all of the following: blood sugar, urea nitrogen, sodium, potassium, chloride, uric acid, cephalin flocculation, hemoglobin, red blood cell count, total white blood cell

count, differential white blood count, erythrocyte sedimentation rate, hematocrit, urinalysis, and determination of urinary 17-hydroxycorticosteroids on the basis of a twenty-four hour collection specimen.

Subsequent to these tests, triamcinolone acetonide was prescribed in the form of a 0.1 per cent adhesive ointment (prepared in Orabase) to be applied four times a day to the acute or chronic mucosal lesions. Thus, it is estimated that approximately 1 Gm. of the ointment was applied each day. Therapy was continued for a period of five days. The amount of the active ingredient, triamcinolone acetonide, which was applied is estimated at approximately 1 mg. per day, or a total of 5 mg. over the five-day period.

Immediately following the conclusion of the period of therapy, the same series of blood and urine studies was repeated for each patient (again in a fasting state). Three of the eleven patients could not serve as their own controls, since the blood and urine examinations were obtainable only after the treatment period.

RESULTS

A comparative study* of the before- and after-treatment blood and urine test values following the five-day period of drug therapy, as described above, did not result in any discernible or noteworthy deviations. All test findings remained within the accepted normal range. Where posttherapy deviations within the normal range were found, no consistent pattern was evident. Such variations as were seen were the kind that would be expected on the basis of routinely observed day-to-day random fluctuations in values or on the basis of variations inherent in repetitive performances of the same test procedure.

In contrast to the previously described inactivity, the benefits usually observed in patients treated with triamcinolone acetonide by topical application in the adhesive vehicle *were* obtained.

No side effects of a clinical nature were observed in any of the patients studied, either during or after experimental therapy.

DISCUSSION

The essentially negative findings concerning systemic activity (as determined by the above-described blood and urine studies) resulting from local applications of triamcinolone acetonide (0.1 per cent) at low dosages are noteworthy in view of this compound's known systemic activity in animals. However, it must be emphasized that the local doses used are admittedly small. It would be hazardous, indeed, to conclude that doses in excess of those investigated in this study would result in similar findings. Furthermore, this investigation did not consider the possible effects of cumulative or prolonged dosages.

*All blood and urine studies reported on here were performed under the direction of Dr. George A. Hyman, Director of the Department of Hematology, Francis Delafield Hospital, to whom we are also indebted for the interpretation of and consultation concerning these data.

SUMMARY

Triamcinolone acetonide, a new corticosteroid which has been suggested as a highly active topical agent in the treatment of certain acute and chronic lesions of the oral mucous membranes, was studied with respect to its possible systemic actions. In order to determine any undesirable effects incident to topical therapy, we undertook detailed blood chemistry, hematologic, and urine studies in eleven patients treated with this corticosteroid.

A comparative study of the before- and after-treatment blood and urine test values following the five-day period of drug therapy (including 1 mg. per day of the active agent, triamcinolone acetonide) did not reveal any discernible or noteworthy deviations. All test findings remained within the accepted normal range. Where posttherapy deviations within the normal range were found, no consistent pattern was evident.

The authors express their appreciation of the assistance of Mrs. Florence V. Moore, Mrs. Aldonna Skislak, and Mrs. Helene W. Kutscher in these studies.

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630 WEST 168TH ST.

THE USE OF TRYPSIN IN THE TREATMENT OF HERPETIC ULCERS IN THE MOUTH

Hugh J. Caven, D.D.S., Wallingford, Pa.

HERPES SIMPLEX is defined as an acute eruptive disorder characterized by the appearance of grouped vesicles on a mildly inflammatory base, accompanied by sensations of heat and burning, and usually occurring about the face. It may involve the mucous membranes.[1]

In the adult the first symptoms of herpes simplex may be soreness or pain in the mouth and throat; bleeding, swollen, and painful gingivae; discomfort on swallowing; enlarged and tender submaxillary glands; and general malaise. Several days later small, rounded vesicles appear anywhere on the oral mucosa, tongue, or lips. The vesicles soon rupture, liberating a clear yellow fluid and leaving raw, painful ulcers with reddened margins. These ulcers may be discrete or confluent.[2]

Acute herpetic gingivostomatitis occurs most frequently in infants and young children, but it may occur in adults. In this clinical entity gingivitis is present, with the gingival tissues presenting an inflamed red appearance. Excessive salivation and constant drooling accompany the condition. A striking feature is an unpleasant odor of the breath. Cervical or submental lymph nodes are enlarged, and this enlargement may persist for days after the lesions have healed.[3]

The pathologic picture of herpes simplex of the oral cavity includes inflammation (heat and redness), edema (swollen gingivae and vesicle formation), and pain.

Crystalline trypsin is indicated in the treatment of inflammation regardless of etiology, according to Innerfield and associates.[4] According to those same authors,[5] the theoretical explanation for the action of trypsin includes (1) enhancement of phagocytosis, (2) lysis of intralymphatic and capillary thrombi, (3) dissolution of fibrin barriers, and (4) amelioration of certain metabolic defects in the area of inflammation.

From a review of the experiences reported by a number of investigators, Moser[6] found that the effectiveness of intramuscular trypsin in the treatment of inflammation and edema associated with thrombophlebitis and other clinical disorders was definitely substantiated.

In inflammation resulting from bacterial invasion or chemical injury, in trauma, and in hematomas, trypsin hastens the resorption of the exudative

or extravasated elements into the blood and lymphatic vessel systems, thus resulting in rapid resolution and healing.[7]

Laboratory studies by Martin and associates[8] showed that prevention of local inflammation and edema is equally effective with cortisone and trypsin; when cortisone alone was used, however, several days pre-treatment was required, whereas the pretreatment time required with trypsin was one-half hour or less.

Laboratory[9] and clinical studies[10a, b] demonstrated that crystalline trypsin could be absorbed through the mucous membrane of the buccal pouch to produce the same degree of clinical response as obtained with parenteral trypsin. Treatment with the buccal tablet obviated the frequent injections needed with the intramuscular form.

Intestinal absorption of trypsin was demonstrated by Martin and associates[11] and confirmed by Bogner and co-workers.[12] They placed "tagged" trypsin into an isolated section of animal intestine and determined its absorption into the blood. These observations led to the preparation of enteric-coated trypsin tablets representing the activity of 20 mg. of trypsin.

Since manifestations of herpes simplex are characterized by inflammation, edema, and pain, it was felt that an anti-inflammatory, antiedema, and pain-relieving agent, such as trypsin, should produce a favorable clinical response. Parenzyme aqueous, 1 ml. representing 5 mg. crystalline trypsin, and buccal tablets of trypsin, each tablet representing 2.5 mg. of crystalline trypsin, were made available for evaluation in the treatment of herpetic ulcers of the mouth and surrounding areas.

MATERIALS AND METHODS

The criteria used for our diagnosis were (1) the clinical picture presented by the patient, (2) a history of acute onset of symptoms, (3) the presence of characteristic lesions, and (4) laboratory studies when deemed necessary.

Of the twenty-two patients in whom trypsin was used, 19 were females and 3 males. Their ages ranged from 3 to 61 years, with an average age of 29.7 years for the group.

Two patients were given intramuscular injections of trypsin aqueous,* one patient was given intramuscular trypsin plus buccal tablets, and nineteen patients received only buccal trypsin.*

The intramuscular trypsin was injected deep into the gluteal muscle. Buccal trypsin was given in doses of one tablet every six hours, to be retained in the buccal pouch or under the tongue until completely disintegrated. The patient was directed not to swallow the saliva during this period but to retain it in the mouth for at least five minutes after the tablet had disintegrated. It was explained to the patient that this was necessary to permit the absorption of the medicine to produce the desired result. Patients were examined daily until a satisfactory response was evident or for a maximum of one week if response was not significant, at which time trypsin treatment was stopped.

*Parenzyme A and Parenzyme B, respectively, products of The National Drug Company, Philadelphia, Pennsylvania.

TABLE I. DATA FOR EACH PATIENT INCLUDED IN THE STUDY

PATIENT	AGE	SEX	DIAGNOSIS	TREATMENT	DURATION OF TREATMENT	SIDE REACTIONS	RESULTS
D. M.	28	F	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	1 day	None	Excellent
S. S.	3	F	Herpetic ulcers	Buccal trypsin 1 q. 8 h.	?	None	Poor
C. W.	13	M	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	3 days	None	Good
G. F.	32	F	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	2 days	Burning tongue	Good
J. B.	42	F	Herpetic ulcers	Parenzyme A (intramuscular), 1.0 c.c. a day for 3 days	Concurrent treatment Cautery—1 week	Pain at site of injection	Poor
J. R.	38	F	Herpetic ulcers	Parenzyme A (intramuscular), 2 doses Buccal tablets 1 q. 6 h.	2 days	None	Good
S. S.	31	F	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	2 days	None	Good
P. S.	22	F	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	2 days	None	Good
A. P.	61	F	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	5 days	None	Fair
M. M.	14	M	Herpetic ulcers	Buccal trypsin 1 q. 6 h.	2 days	None	Good
R. M.	40	F	Ulcers on palate	Buccal trypsin 1 q. 6 h.	2 days	Ulcers worse	Poor
W. M.	40	F	Recurring herpetic ulcer	Buccal trypsin 1 q. 6 h.	Unable to contact patient for follow-up		
J. H.	39	F	Oral and nasal herpetic ulcer	Buccal trypsin 1 q. 6 h.	1 day	None	Excellent
W. H.	35	F	Herpetic ulcer (3 weeks)	Buccal trypsin 1 q. 6 h.	Unable to contact patient for follow-up		
E. M.	38	F	Herpetic and decubitus ulcers	Buccal trypsin 1 q. 6 h.	2 days	None	Good
W. M.	25	F	Recurring oral and nasal herpetic ulcer	Buccal trypsin 1 q. 6 h.	5 days	None	Fair
B. D.	14	F	Herpetic ulcer	Buccal trypsin 1 q. 6 h.	3 days	None	Good
J. H.	48	M	Herpetic ulcer (1 week)	Buccal trypsin 1 q. 6 h.	2 days	None	Good
J. M.	34	F	Herpetic ulcer	Buccal trypsin 1 q. 6 h.	1 day	None	Excellent
S. D.	5	F	Herpetic ulcer on lip	Buccal trypsin twice daily	1 day	Rapid improvement after 1 tablet	Excellent
B. B.	55	F	Herpetic ulcer, swollen jaw after extraction of 2 abscessed teeth	Parenzyme A, 1.5 c.c. IM	2 days	Pain at site of injection	Excellent
W. M.	25	F	Large herpetic ulcer on external nares (1 week)	Buccal trypsin 1 q. 6 h.	2 days	None	Excellent

RESULTS

The type and duration of treatment and the results obtained are shown in Table I.

It will be observed that the results are rated as excellent, good, fair, and poor. Excellent results, in which the lesions were healed in one or two days, were observed in six patients. Good results, in which the lesions were healed in two to three days, were observed in nine patients. Fair results, in which the lesions were healed in five days, were observed in two patients. Poor results, in which there was no improvement within one week or the condition was made worse, were observed in three patients. Two patients failed to return for follow-up, and therefore no results are recorded for them.

SUMMARY AND CONCLUSION

Nineteen patients with herpetic ulcers in the mouth were treated with buccal tablets of trypsin. Excellent results were obtained in five patients, good results in eight, fair results in two, and poor results in two. Two patients failed to return for follow-up.

Two patients were given intramuscular trypsin. One was treated for three consecutive days with poor results; the other received one injection and obtained an excellent response.

One patient was treated with intramuscular trypsin for two consecutive days and with buccal trypsin between injections. A good response was obtained in this patient.

One patient taking the buccal tablets complained of a "burning" sensation of the tongue. Two patients given parenteral trypsin complained of pain at the site of injection.

The foregoing results seem to establish a rationale for the use of trypsin, either buccal or parenteral, in the treatment of herpetic ulcers of the oral cavity. The rapid control of symptoms and the fast disappearance of the lesions in many of the cases suggest this therapeutic procedure in herpes simplex.

Addendum: After this report was completed, six patients with herpetic ulcers were treated with an enteric-coated trypsin tablet representing the activity of 20 mg. trypsin. Two tablets every six hours for three doses daily were prescribed. The results were good to excellent. The oral tablets are easier to take and assure the practitioner of cooperation from the patient.

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ORAL ROENTGENOLOGY

American Academy of Oral Roentgenology

Arthur H. Wuehrmann, Editor

PANTOMOGRAPHY AND ORTHOPANTOMOGRAPHY

Yrjö V. Paatero, D.Odont., Helsinki, Finland

PANTOMOGRAPHY

THE term "pantomography" is a contraction of the words "panoramic tomography." I have used it since 1950. The method is based on the principle that a sharp image of a rotating object (in practice, a thin layer which is immobile in relation to the film) is projected upon a lineally moving or rotating film when the tissue surfaces (or layer) and film are exposed by a narrow x-ray beam. The surface and the film must move through the beam with an equal linear velocity. It makes no difference whether during exposure the object rotates between the x-ray tube and the film or the tube and the film circulate around the object. The coordinated movement of the factors must be definitive. This basic principle of pantomography was pointed out in my patent application in 1950.[4] It has been referred to many times in subsequent publications.

After early experiments in Finland, I published a preliminary paper on the new method in 1949.[3] The prototype of the pantomograph for roentgenography of living subjects was built in 1950, when I was further developing the method during the one and one-half years that I spent at the School of Dentistry, University of Washington, Seattle, Washington. Fig. 1 depicts the instrument's development just prior to my return to Finland in 1951. A rotating film in a flexible cassette was used. Lineally moving film was used also on a temporary basis. In spite of the rather primitive construction of the apparatus, the resulting pictures ("pantomograms") were sometimes encouraging. Such films may be seen in Figs. 2 and 3. Fig. 2 is a so-called concentric pantomogram of a 7-year-old girl; Fig. 3 is a double-eccentric pantomogram of an adult subject. The function of the panoramic x-ray machine developed by

From the Roentgen Department (Director: Prof. Dr. Yrjo V. Paatero), Institute of Dentistry, University of Helsinki, Finland.

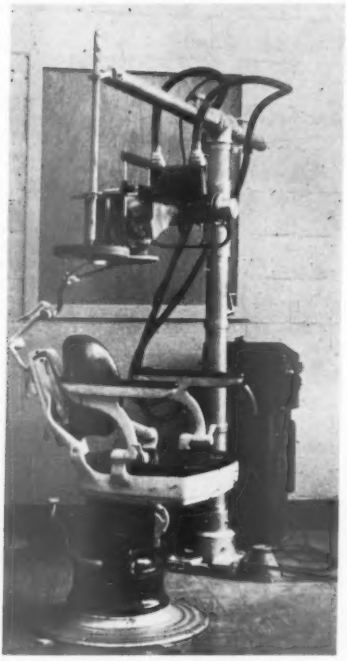

Fig. 1.—An early pantomograph set up in 1951 at the School of Dentistry, University of Washington.

Fig. 2.—Concentric pantomogram of the jaws and facial bones of a 7-year-old girl, taken in 1951 with the apparatus shown in Fig. 1.

the United States Air Force seems to be based on the double-eccentric technique.[2] As far as I know, in England they use mainly the concentric exposures.[1] Their apparatus is equipped with a rotating cassette holder.

If a concentric pantomogram is to be taken, the object (in this case the jaws) should be positioned symmetrically to the rotation axis. Usually the best reproduction of the condyles and the entire temporomandibular joint is obtained if the rotation axis is approximately 1 cm. dorsally to the vertical plane which goes through both condyles. If such a location is used, the resulting film shows much overlapping of the molars and premolars. This disadvantage may be eliminated markedly by moving the subject's head somewhat backward, so that the rotation axis will be between the third molars.

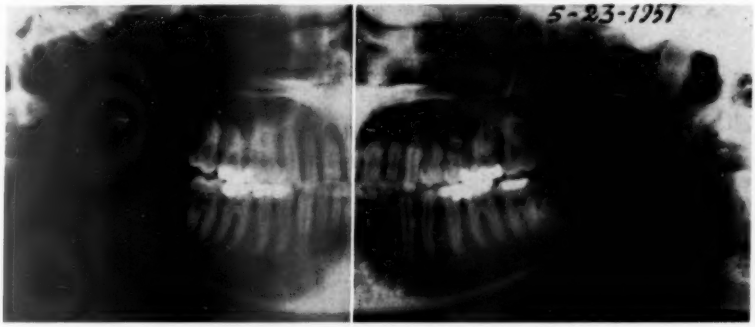

Fig. 3.—Double eccentric pantomogram of an adult patient, taken in 1951 with the apparatus shown in Fig. 1.

In order for all the teeth to appear uniformly well defined, it is necessary to use the eccentric technique. Thus, each side of the face is roentgenographed separately. The head is positioned for the eccentric exposure in such a way that the rotation axis is located approximately at the third molar on the right side when the left side of the maxilla and mandible is to be reproduced, and vice versa. Thus, the projection is nearly orthoradial over the entire premolar and molar region. Only the incisive areas appear in oblique projection. Two positionings of the patient and two exposures are needed. The exposures may be made on two separate films or on a single film. Both concentric and eccentric techniques have been used at our Institute during the last ten years. The construction and use of the apparatus have been explained in detail in several earlier articles.[5-10] Other non-English articles are also available.

The very early experiments showed that stereoscopy is suitable for use in pantomography.[9] Whenever required, routine pantomograms can be taken stereoscopically. For example, the possible dislocation of fragments of a fractured mandible or maxilla can be easily demonstrated when this added refinement is used.

Instead of a single film, two or more films may be used in the same or separate cassettes. Each film picks up an image of that surface whose shape

and location are in optimum relation to the rotational axis of the film. Hence, it is possible to roentgenograph simultaneously several thin layers whose shapes may be different.

ORTHOPANTOMOGRAPHY

In order to obtain an orthoradial pantomogram of the entire dentition (that is, in such a way that the narrow x-ray beam penetrates the entire tooth-bearing area of both upper and lower jaws perpendicularly), I tried to combine the concentric and eccentric exposures on a single film, using a single exposure.

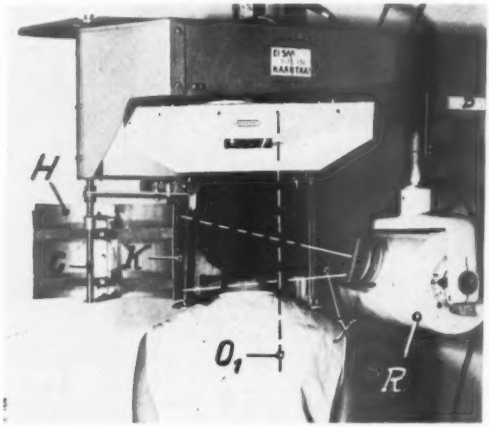

Fig. 4.—Orthopantomograph at the Institute of Dentistry, University of Helsinki. The rotational movement of the machine occurs successively about three rotation axes. Note the x-ray tube *(R)* and the rotating curved cassette holder *(H)* with the flexible plastic cassette *(K)* at the starting position of exposure. When the left side of the jaws is in focus, the narrow x-ray beam *(X)* turns about axis O_1. (Exporter: Oy Sarjavalmiste Ab. Helsinki, Finland.)

Both theoretical study and preliminary experiments were positive as early as 1954.[10] In 1958 I returned to this problem and built a miniature apparatus, an "Orthopantomograph," for experimenting with dry skulls.[11] The results were so encouraging that I received a grant for building a prototype for roentgenography of living subjects.[12] In this apparatus (Figs. 4 and 5) the patient sits immobile while the x-ray tube (*R*) and the curved cassette holder (*H*) with a plastic cassette (*K*) circulate around his head. Concurrently, the cassette holder rotates about its own rotation axis (*C*). The tube and the axis of the cassette holder are attached to a horizontal bar (*D*) which turns successively about three rotation axes (O_1, O_2, and O_3). Numbers *1* and *1'* denote the starting positions of the x-ray tube and the axis of the cassette. The narrow x-ray beam (*X*) is in the same vertical plane as the bar (*D*) (Fig. 4) and turns about axis O_1 to positions *3* and *3'*. The axis (*C*) has moved simultaneously along the curve (*T*), the shape of which corresponds to the shape of the dental arch (*S*). As soon as the beam has reached point *P*, which corresponds approximately to the location of the left second premolar, axis O_1 is released and the rotation

movement of the x-ray beam continues about axis O_2 until point N is reached. At this time the x-ray beam begins rotating about axis O_3. When the tube is in position *4* and the cassette in position *4'*, the first half of the film is exposed (the blackened part in Fig. 5). The linear velocity of the film must be equal to the relative velocity of the dental arch (curve *S*) as the x-ray beam passes through it. It makes no difference whether the tube and the cassette circulate around the object, as in the present apparatus, or whether, as in the miniature apparatus,[11] the object moves between the said factors.

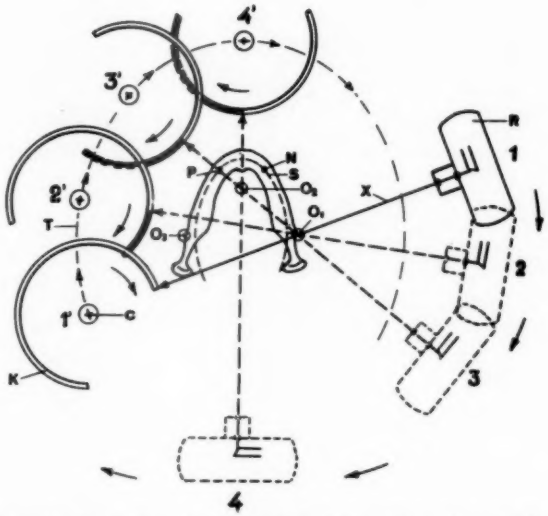

Fig. 5.—Schematic illustration of the function of the orthopantomograph shown in Fig. 4. The x-ray beam *(X)* turns about axis O_1 when the left side of the jaws is being reproduced on the film, and about axis O_2 when the front part *(PN)* is in focus. Axis O_3 is in use as the rotation center when the right side of the face is exposed.

Regardless of a little uneven change of the axes in the present prototype, the resulting orthopantomograms are remarkably good. The results may be seen in Figs. 6, 7, and 8. In my opinion, pictures like these may be of great significance in various aspects of dentistry and medicine. This does not mean that ordinary intraoral and extraoral roentgenograms will not be necessary in the future.

Orthopantomograms may also be taken stereoscopically. Both vertical and horizontal tube shifts may be used.[13] Stereoscopic views may be obtained with a single exposure of the entire jaws.[7, 14] Two films can be exposed simultaneously from slightly different angles with a single source of rays. The stereoscopic effect can be achieved even if only one of the double films is exposed with a slightly oblique x-ray beam. In practice, this occurs when the entire x-ray beam reaches the outer film but only half of the beam reaches the inner film. One film thus receives a slightly oblique projection in relation to the other film. There is a gap of approximately 4 mm. between the two cassettes.

Within this space a vertical metal (lead) strip protects the horizontally moving inner film from one half of the x-ray beam. A special cassette holder, designed to carry two cassettes, has been used when single-exposure stereoscopic orthopantomograms were taken. This has recently been described in detail.[14]

Fig. 6.

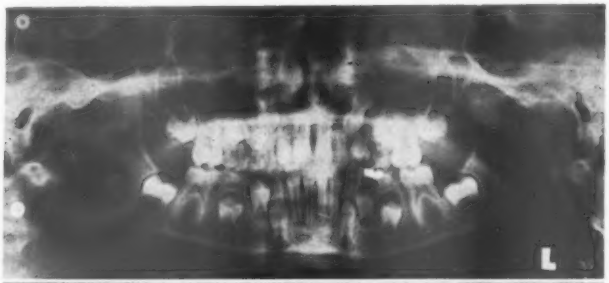

Fig. 7.

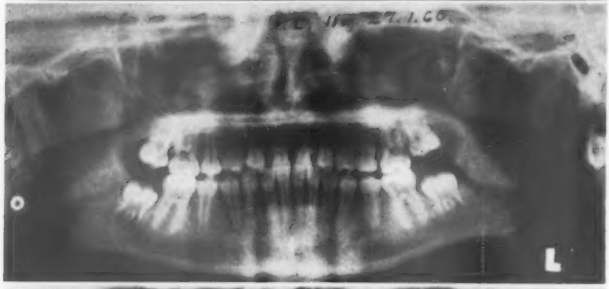

Fig. 8.

Fig. 6.—Orthopantomogram of a normal 7-year-old child.
Fig. 7.—Orthopantomogram of a normal 11-year-old child.
Fig. 8.—Orthopantomogram of an adult with a pathologic condition.

As for the concentration of radiation dose in orthopantomography, the maximum exposure seems to occur at the three rotation axes. This has been shown in accordance with the technique of Vuorinen.[15] More exact measurements will be accomplished in the near future.

Voltage is an important factor in pantomographic methods. In orthopantomography, 85 KVP seems to suffice. With approximately 13 Ma., the exposure time for the entire ear-to-ear roentgenogram is 15 to 20 seconds. The exact time is dependent on the thickness of the object and the half-value layer of the beam. The tube ordinarily used has a 1.8 mm. focal spot.

SUMMARY

The development of the pantomographic method from its earliest stage to the present has been described. The new apparatus, the Orthopantomograph, utilizes three separate rotational axes; the "old" method is based on a single rotational axis. By means of the three axes, it is possible to make orthopantomograms, that is, the entire tooth-bearing area of the maxilla and mandible is projected on the film orthoradially and perpendicularly. Stereoscopy is adaptable in pantomography, even with a single exposure.

The development of the pantomographic methods has been supported at different times by the University of Washington, Seattle, Washington; the United States Federal Security Agency; the United States Public Health Service; Hammasväline Oy, Helsinki; Lääkintäsähkö Oy, Helsinki; the Sigrid Juselius Foundation, Helsinki; the Cultural Fund of Finland, Helsinki; the State Scientific Board, Helsinki; the Finnish Dental Society, Helsinki; and the Emil Aaltonen Foundation, Tampere.

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THE UNIVERSAL U AND L BITE-BLOCK FILM HOLDER

A Method of Positioning and Holding Intraoral X-ray Films for Both Maxillary and Mandibular Exposures

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THE problem in placing maxillary intraoral x-ray films has produced a variety of film holders. The most important considerations which each is attempting to incorporate are (1) proper position, (2) proper angle (as nearly parallel to the long axis of the tooth as possible), (3) stability of the film during exposure, (4) prevention of film bending, except where intended, (5) the patient's comfort, (6) simplicity of application, (7) adaptability to mandibular teeth as well as to maxillary teeth, and (8) ease of sterilization.

The digital method of holding the film in place is probably the most universally used, but it often fails because the patient may inadvertently move or bend the film. The position is usually far from being parallel to the long axis of the tooth. This method also involves unnecessary exposure of the patient's hands to x-radiation. In addition, there is the slight inconvenience of having the patient wash his hands before putting his fingers into his mouth.

Plastic or wooden bite-block film holders which depend on friction to hold the film in place in the block do not furnish the required stability, they sometimes fail to establish the proper angle, and they do not always satisfy such sterilizing requirements as boiling or autoclaving. Some operators can obtain good results with a hemostat, but when an instrument as long as a hemostat is used any movement of the patient's hand results in an accentuated movement of the film.

At Indiana University School of Dentistry, the successful use of a thumbscrew bite block in taking roentgenograms of the mandibular teeth has stimulated the production of a thumbscrew type of bite-block film holder for use on the maxillary teeth as well as on the mandibular teeth. This thumbscrew method of holding the film in the block makes it possible to alter the position of the film in the block to compensate for irregularities of the various mouths; it also accommodates films of different thicknesses and different sizes with greater ease. The thumbscrew type of bite block (Fig. 1) consists of a rather long extension of the biting block; it has a bend of 18 degrees. This bend makes it adaptable

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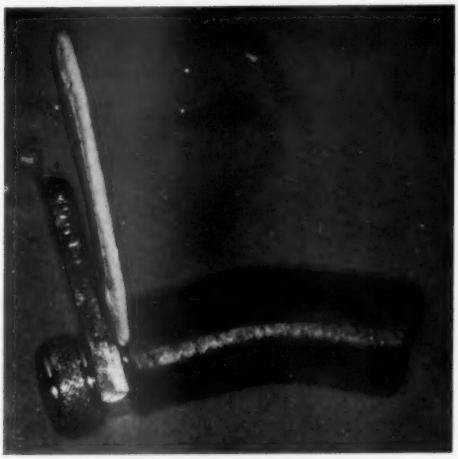
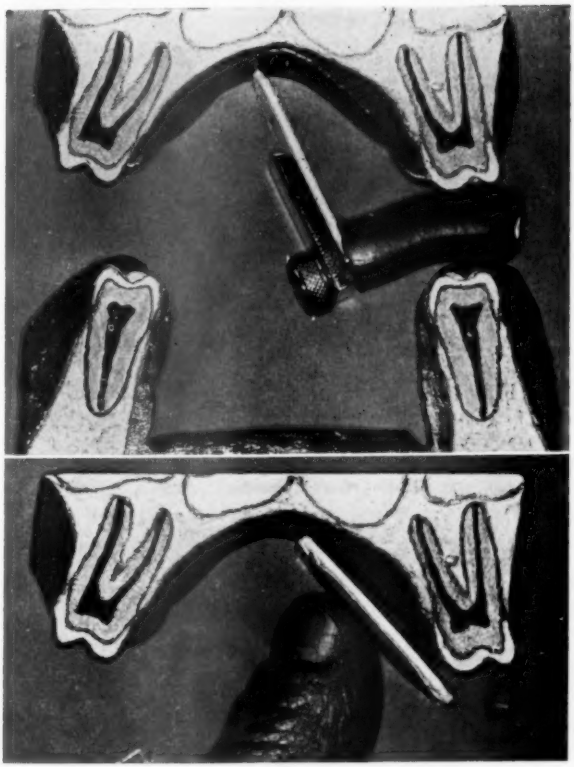


Fig. 1.

A.

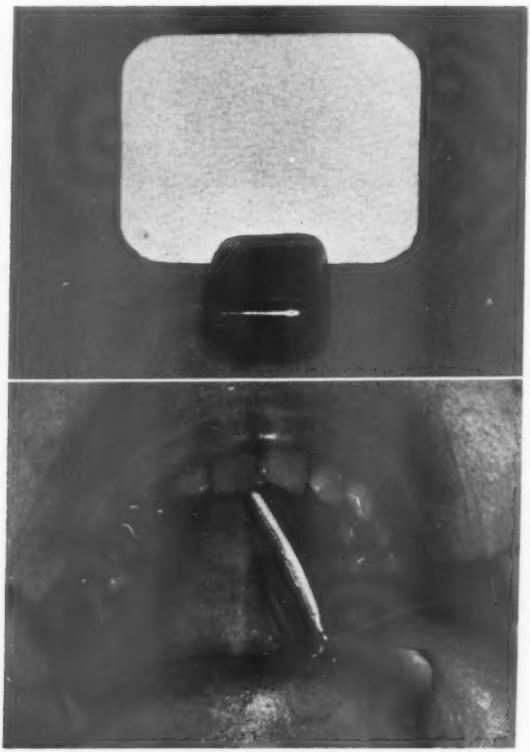


B.

Fig. 2.

to both maxillary and mandibular arches and satisfies most of the other requirements of an ideal bite-block film holder. The film is maintained in position by a metal film backing. This metal plate is tightened to the film by means of a thumbscrew. The angle of the film, when the thumbscrew film holder is used, is not always parallel to the long axis of the tooth in the maxillary arch in all mouths, but the film position is a definite improvement over that obtained with the digital method of support. Fig. 2 contrasts film placement in the maxilla by the two methods.

A.



B.

Fig. 3.

The stability of the block is a distinct advantage, and the block is definitely more comfortable to the patient than other film holders. Since the angles of x-ray beam projection are more nearly horizontal in the maxillary areas when the bite-block film holder is used than when the film is held by the digital method, the shadow of the zygoma on the posterior films is more adequately eliminated in most mouths.

The extension of the biting surface of the bite block is long enough that the film can be properly positioned with the biting surface against the occlusal plane

of the teeth in the arch being examined. If, when the patient closes his jaws on the bite block, the film rotates because of irregular occlusion, the position of the film in the block can be changed to correct the placement situation. Partial dentures in the opposite arch may be left in place to stabilize the film and the holder.

The film used for the maxillary molars is not bent and is placed horizontally in the bite block, slightly to the anterior of the middle of the film. Fig. 3, *A* illustrates the proper placement of the film in the holder for maxillary molar

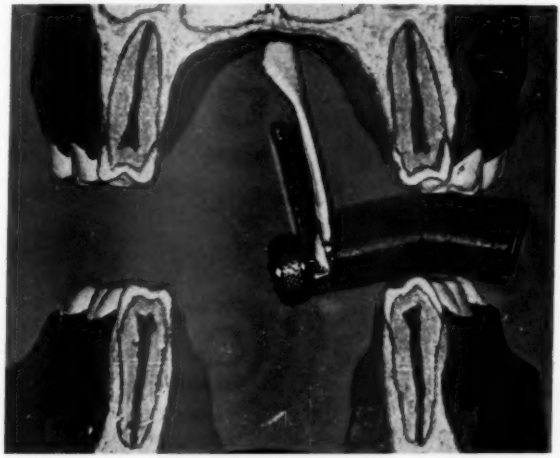


Fig. 4.

exposures. If the curve of Spee is great, the film, when grasped in the holder, may be tilted up slightly toward the posterior. The superior edge of the film is placed near the midline of the palate, and the bite plane of the bite block is placed against the maxillary teeth (Fig. 3, *B*). The patient is then instructed to close his jaws against the bite block. This action will hold the film securely in place.

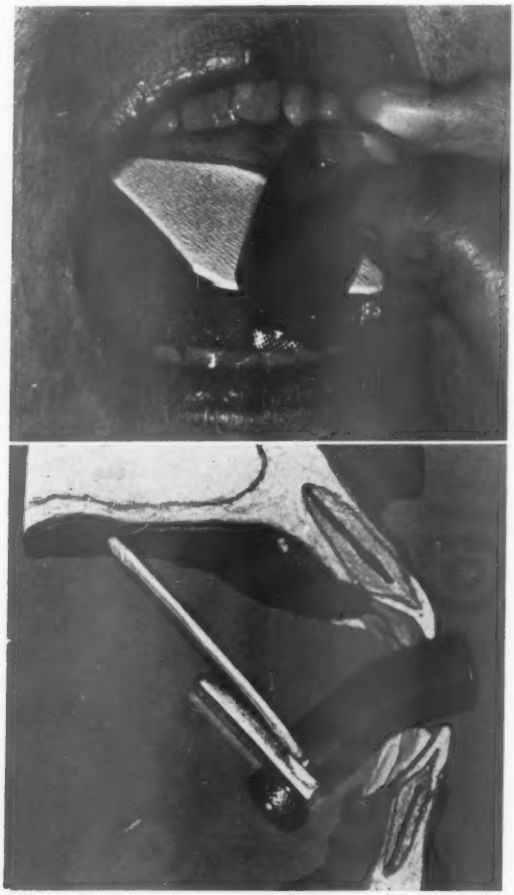
In the maxillary premolar exposure, the anterior superior corner of the film is deliberately bent to conform to the anterior curve of the palate. The rest of the placement is similar to that for the maxillary molar. Fig. 4 demonstrates film placement in the maxillary premolar region. Stone models cut through the premolars at right angles to the sagittal plane are used in this illustration.

In placement of film for the maxillary cuspid exposure a bend at the mesial superior edge of the film will be required if the palate is narrow, but in most mouths this bend is unnecessary. The incisal edge of the maxillary cuspid and lateral incisor should contact the bite block near the outer end of the block. This positions the lower edge of the film away from the incisal edge of the cuspid and thus results in a more nearly parallel position of the film-tooth relationship. Film positioning in the maxillary anterior areas is shown in Fig. 5.

Film placement for the maxillary incisor exposure does not require any bend in the film, except in very narrow arches. No. 1 films may be preferable in these cases. As in the cuspid exposures, the incisal edges of the central incisors should also be near the end of the block.

This longer bite block has definite advantages in positioning films for mandibular exposures. For the molar film positioning, the block is attached to the anterior third of the film so that the film can extend as far distally as possible, and the film is tilted up at the posterior end in order to compensate for the curve of Spee. The tongue is depressed with a finger, and the film is placed properly in position before the patient is instructed to close his jaws on the block. The block is usually grasped by the second molars for this exposure. Fig. 6 illustrates mandibular molar film placement.

A.



B.

Fig. 5.

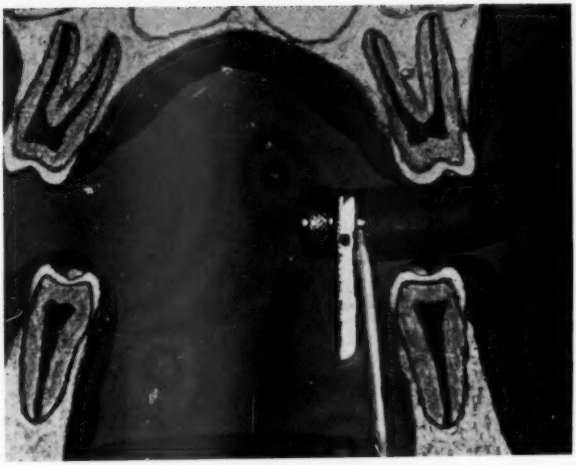
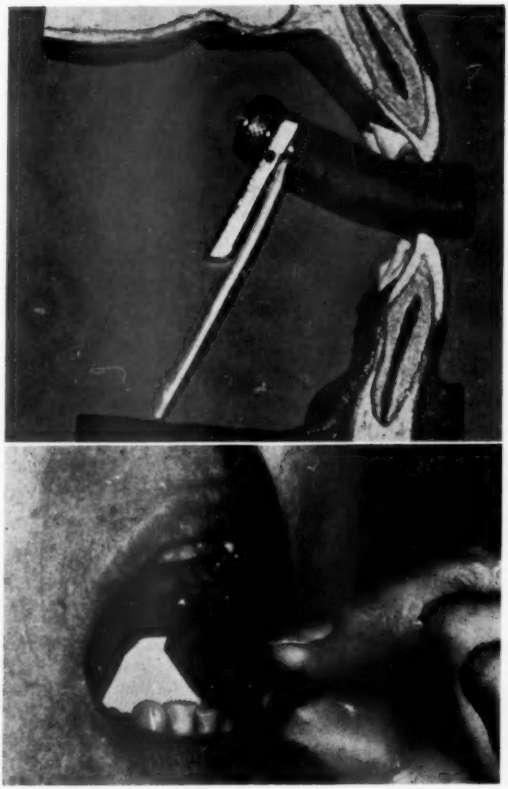


Fig. 6.

A.



B.

Fig. 7.

The premolar film is placed horizontally in the block, and as the tongue is depressed the film is placed in the mouth with the block at the second premolar area. The technique is essentially similar to that for the molar area.

The film for the mandibular cuspid exposures is placed vertically in the block toward the mesial border of the film. Again the tongue is depressed and the inferior edge is placed as far back toward the base of the tongue as possible. The superior edge is moved away from the incisal edges of the teeth, so that the patient can close his jaws on the outer edge of the block. In many mouths, this creates an almost parallel tooth-film relationship.

This longer bite block is also advantageous for the mandibular incisor exposures. It is positioned much like the cuspid film, except that the block is placed in the middle of the film. The longer extension allows the film to be far enough back in the mouth that a full-sized intraoral film can be used, even in the most narrow mouths. A nearly parallel tooth-film relationship is usually accomplished. Fig. 7 illustrates film positioning in the mandibular anterior area.

CONCLUSIONS

The thumbscrew bite-block not only satisfies the requirements of an ideal bite block, as outlined earlier in this article, but also has the following additional advantages:

1. Less time is required for instruction of patients in order to secure their cooperation.
2. Radiation to the patient's hands is reduced.
3. This method is more comfortable for the patient. The stability of the block reduces stimulation of the gagging reflex.
4. Students and technicians can be taught the method in a very short time with excellent results.

ROENTGENO-QUESTIONS

What are the advantages of a "long cone" on a dental machine?
Several advantages accrue from the use of a long cone:

1. The entrance skin dose is lower and the exit skin dose is higher.
2. There is better definition and less enlargement of the roentgen image, regardless of the method of positioning the film packet in the patient's mouth.
3. Longer exposure times are required, permitting the use of high-speed films without changing mechanical exposure-timing devices now in use on late-model x-ray equipment.
4. There is less tissue within the primary beam of radiation, since there is less spreading of the x-ray beam.

What is the minimal amount of radiation that will do harm to a patient? (Please answer as if to a patient.)

There is great danger of misunderstanding between the dentist and the patient concerning the dentist's answer to this question. Any answer should be phrased for the individual patient. This answer should take into consideration the patient's knowledge of ionizing radiation and his ability to understand the general problem.

If the patient has no knowledge of ionizing radiation, it is probably best simply to state that it has never been shown that dental x-rays made in dental offices are harmful to the patient. (In this instance, the word "harmful" refers to clinical evidence of radiation damage.)

If the patient has some knowledge of ionizing radiation and is aware that no dose of x-radiation can be called "safe," then the dentist's answer should probably emphasize the fact that the benefits resulting from the use of x-radia-

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The American Academy of Oral Roentgenology solicits from the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY any questions which deal with technical or interpretive aspects of oral roentgenology. These questions should be sent directly to the editor of this section, Dr. Arthur H. Wuehrmann, School of Dentistry, University of Alabama Medical Center, Birmingham, Alabama; the editor will distribute them for reply to a suitable group within the Academy. Questions, with the answers, will be published at as early a date as possible in "Roentgeno-Questions." Questions, especially those of an interpretive nature, should ordinarily be accompanied by good-quality roentgenograms and a pertinent history. The names of the questioner and the respondent will not be published.

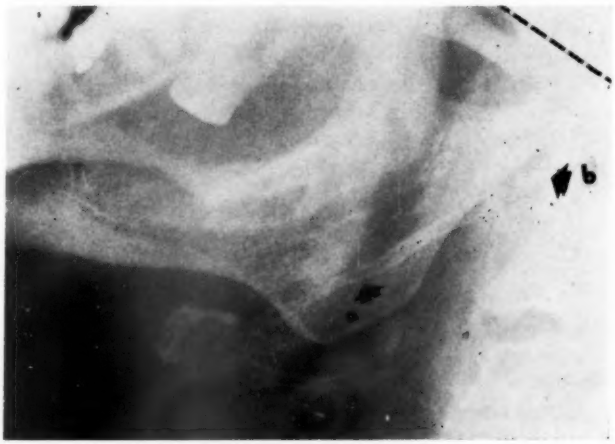
tion outweigh any possible damage. A good example of this is the use of x-radiation in the treatment of cancer or the use of many x-ray films in the diagnosis of a fracture case.

If the patient understands ionizing radiation, the dentist is forced to answer that any dose other than zero can cause some change and that this change will be detected if laboratory tests of suitable sensitivity can be employed. Any answer that the dentist gives such a patient must include both genetic and somatic effects of irradiation and also the difference between specific area irradiation and whole body irradiation. This is necessary if the patient is to understand the hazards of dental x-radiation.

ROENTGENO-ODDITIES

Calcified Stylohyoid Ligament

EXAMINATION of the accompanying roentgenogram reveals a lateral oblique view of the mandible, the hyoid bone, and the anterior aspects of the cervical vertebrae. Posterior to the body of the hyoid, one observes a bonelike structure (*a*) measuring approximately 3 mm. in thickness and 5.5 cm. in length. This structure runs from the region of the lesser cornu (of the hyoid bone) and appears to contact the vertebral column. It is not a commonly observed anatomic entity. At first glance, it does not appear possible that this could be a calcified stylohyoid ligament, for it seems to be attached to a vertebra rather than to



Each month this section will bring to the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY one or more roentgenograms which demonstrate unusual, unexpected, rare, or bizarre roentgenographic changes. These roentgenograms will be accompanied by an explanation or by words of inquiry regarding the particular change. All films used in this section will be accepted with the understanding that 2 by 2 or 3¼ by 4 inch slides or glossy photographs of the films will be made available to interested readers through the editor of the American Academy of Oral Roentgenology at the individual's expense. The cost will involve only the photographer's charges. Each slide or print will give credit to the donor. Interesting roentgenograms are solicited from all sources. Please be certain to identify your films properly so that they can be returned. All material for publication should be submitted to Dr. Arthur H. Wuehrmann, University of Alabama School of Dentistry, Medical Center, Birmingham, Alabama.

the styloid process. (The styloid process is a part of the temporal bone and is located posterior and just slightly medial to the center of the articular fossa.) However, if one uses the zygomatic arch (see dotted line) as a landmark to approximate the level of the base of the skull, it can be observed that the structure (*b*) to which the linear calcification is attached does extend downward and forward in a manner consistent with the usual appearance of the styloid process.

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Brookline, Mass.

ORAL PATHOLOGY

American Academy of Oral Pathology

Donald Kerr, Editor

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OBSERVATIONS ON THE EXFOLIATIVE CYTOLOGY AND HISTOLOGY OF THE ORAL MUCOUS MEMBRANES IN IRON DEFICIENCY*

Raymond W. Monto, M.D., Rafael A. Rizek, M.D., and Gerald Fine, M.D., Detroit, Mich.

THE oral mucosal membranes, particularly those of the tongue, although excellent indicators of the constitutional state of the patient, are seldom diagnostic of specific systemic disease. Gross anatomic abnormalities of the lingual mucosa have been observed by clinicians for many years. Symptoms of glossitis are associated with many deficiency states, including pernicious anemia, iron-deficiency anemia, sprue, pellagra, malnutrition, pregnancy, and certain sensitivity reactions to drugs and physical agents. The pathophysiologic mechanisms in these diseases are poorly understood.[1-3] The present study was undertaken to evaluate the mechanism involved in the production of glossitis and atrophy of the squamous-cell epithelium of the mucosa of the tongue in patients with classic iron-deficiency anemia.

MATERIAL AND METHODS

Five patients met the clinical and laboratory criteria of moderately severe iron-deficiency anemia with glossitis in this investigation (Table I). Exfoliated cells of the tongue and buccal mucous membranes were obtained by the following method. First, to remove excess debris and bacteria within the oral cavity, the mouth was rinsed with water. The squamous epithelial cells of the tongue were obtained by gently stroking the dorsal surface of the tongue with the edge of a regular 3 by 1 inch laboratory glass slide. The specimen was then smeared with a second glass slide. The preparations were immediately immersed and fixed with 95 per cent alcohol and stained by the usual method of Papanicolaou.

From the Department of Medicine, Division of Hematology and Department of Laboratories, Henry Ford Hospital, Detroit, Michigan.

*The second Helen McLain lecture, presented before the American Academy of Oral Pathology in April, 1960.

TABLE I

CASE NO.	PATIENT	AGE	DIAGNOSIS	DIET	HEMOGLOBIN (GM. PER CENT)	RED BLOOD CELLS (10^6)	HEMATOCRIT (PER CENT)	RED BLOOD CELL MORPHOLOGY	SERUM IRON (MG. PER CENT)	HEMOGLOBIN AFTER IRON THERAPY	
										MONTHS	GM. PER CENT
1	W. F.	47	Plummer-Vinson syndrome	Poor	7.7		29	Microcytic hypochromic	27	2 12	12.2 12.7
2	W. M.	61	Carcinoma of stomach	Adequate	8.2	3.84	28	Microcytic hypochromic	26	3 7	12.9 12.7
3	W. F.	57	Hiatus hernia	Adequate	7.0		29	Microcytic hypochromic	30	3 11	12.2 12.5
4	W. F.	44	Hemorrhagic disorder	Adequate	6.9	3.39	25	Microcytic hypochromic	44	4 10	11.5 11.8
5	W. F.	77	Carcinoma of rectum	Poor	6.9		26	Microcytic hypochromic		2 12	12.3 12.6

A similar technique was used to obtain the specimen from the buccal mucosa. In a few patients, exfoliated cells were procured from the stomach, the vagina, and the cervix uteri. Second, clinical photographs of the extruded tongue were taken. Third, using a surgical microscope, we observed the anterior dorsal surface of the mucosa of the tongue for the presence or absence of mucosal and papillary atrophy. Fourth, a surgical biopsy of the tongue was performed.

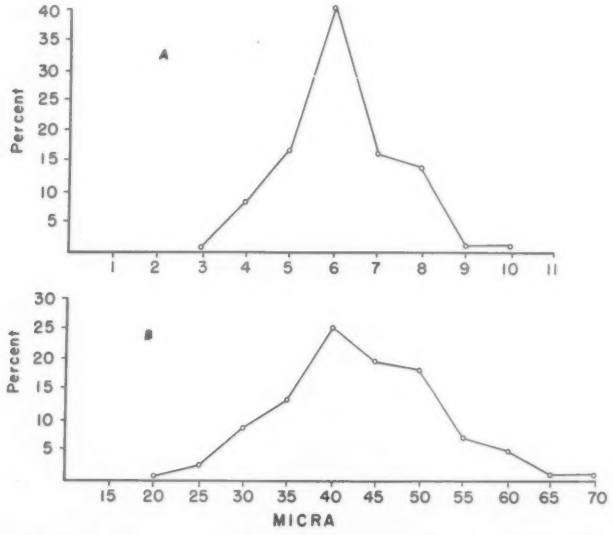


Chart 1.—The distribution of exfoliated squamous epithelial cells of the tongue in normal subjects measured in the longest diameter. *A*, Nucleus; *B*, cytoplasm.

These procedures were performed before, during, and after completion of iron therapy. Selected specimens were studied for ribonucleic acid (RNA) and glycogen content.

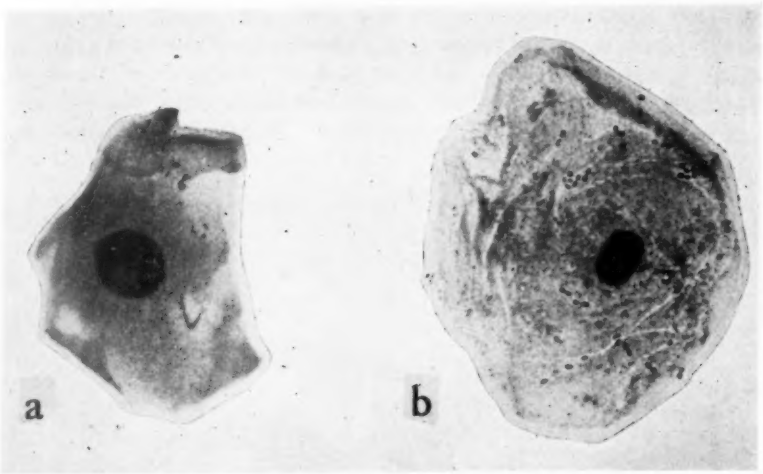


Fig. 1.—Exfoliated precornified cell *(A)* of the tongue in iron-deficiency anemia. The cytoplasmic diameter is reduced, and the nucleus is enlarged and rounded. The chromatin pattern is bizarre, with fine stippling of nuclear material and increase in nucleoli. After iron therapy, the cell returns to normal *(B)*. (Magnification, ×1,000.)

RESULTS

Observations on the exfoliated cells from five normal persons between 35 and 55 years of age (two men and three women) were first evaluated. The exfoliated cells obtained from the lingual mucous membrane were of the following types: basal, parabasal, precornified, cornified, and keratinized. In normal persons 60 to 80 per cent of the exfoliated cells were of the cornified epithelial type. Approximately 10 to 35 per cent were from the precornified layers and 5 to 10 per cent were keratinized. A few scattered cells from the basal and parabasal areas were infrequently observed. The cells were studied at a magnification of ×1,000. In each subject 100 epithelial cells were studied at random. Observations were made with respect to the longest diameter of the cytoplasm and the nucleus, and notations were made as to structure of both the cytoplasm and the nuclei. A composite of the observations was obtained in normal persons and depicted by a Price-Jones type of curve as shown in Chart 1. It is noted that the largest diameter of the cytoplasm falls between 30 and 55 micra in more than 90 per cent of the cells. The nuclei observed were usually oval in shape and pyknotic in character, measuring 4 to 8 micra in longest diameter (Fig. 1, *B*). Abnormalities, such as reticulation of the nuclear pattern, nucleoli, karyolysis, double nuclei, or bizarre forms, were encountered very rarely. The nuclear pattern was found to be fine and homogeneous. The cytoplasm to nucleus ratio was noted to be approximately 7 or 8 to 1. The exfoliated

cells from the buccal mucosa, in general, demonstrated slightly larger cytoplasmic and nuclear size than most specimens obtained from the tongue. There was no keratinization, and relatively fewer cornified cells were present.

Chart 2 illustrates a Price-Jones curve obtained from measurements of nuclei and cytoplasm in one of our patients before iron therapy, after six weeks of treatment, and at the end of one year. The specimens taken from the tongue mucosa in this patient (Fig. 1, *A*) illustrated the type of exfoliative cells obtained before therapy. There was a reduction in the total diameter of the cytoplasm, the borders of which were round with a paradoxical increase in the

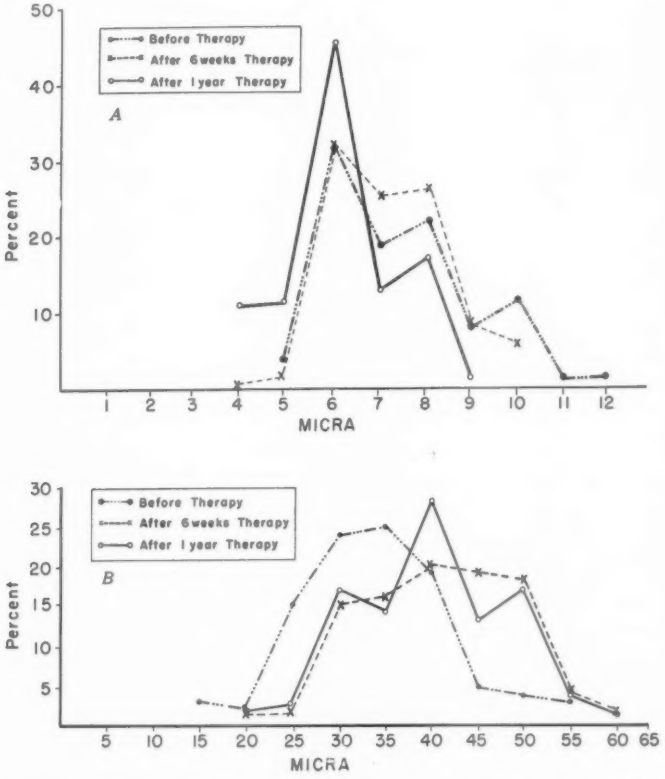


Chart 2.—The distribution of exfoliated squamous epithelial cells of the tongue in a patient with iron-deficiency anemia measured in the longest diameter before, during, and after iron therapy. *A*, Nucleus; *B*, cytoplasm.

nuclear size, thus altering the cytoplasm to nucleus ratio. The "microcytosis" of the exfoliative squamous epithelial cells of the tongue is reminiscent of the microcytes of the circulating red blood cells. A minimal enlargement in nuclear diameter can result in a considerable increase in nuclear volume, estimated to be tenfold in some instances. Certain qualitative changes were observed. These

consisted of a bizarre nuclear pattern associated with fine stippling of nuclear material and an increase in nucleoli. Binucleation and occasional karyorrhexis were found in numbers not seen in normal subjects. In the stomach washing, the columnar cells were essentially normal in appearance in one subject studied. The cervical and vaginal smears showed changes similar to those observed in cells from the oral cavity. Following iron therapy there was a reversal of the aforementioned abnormalities. Spheroidal pretreatment nuclei became smaller, pyknotic, and oval. The cytoplasmic nuclear ratio returned to normal values. The cytoplasm of the cells approached normal diameter with sharp cytoplasmic

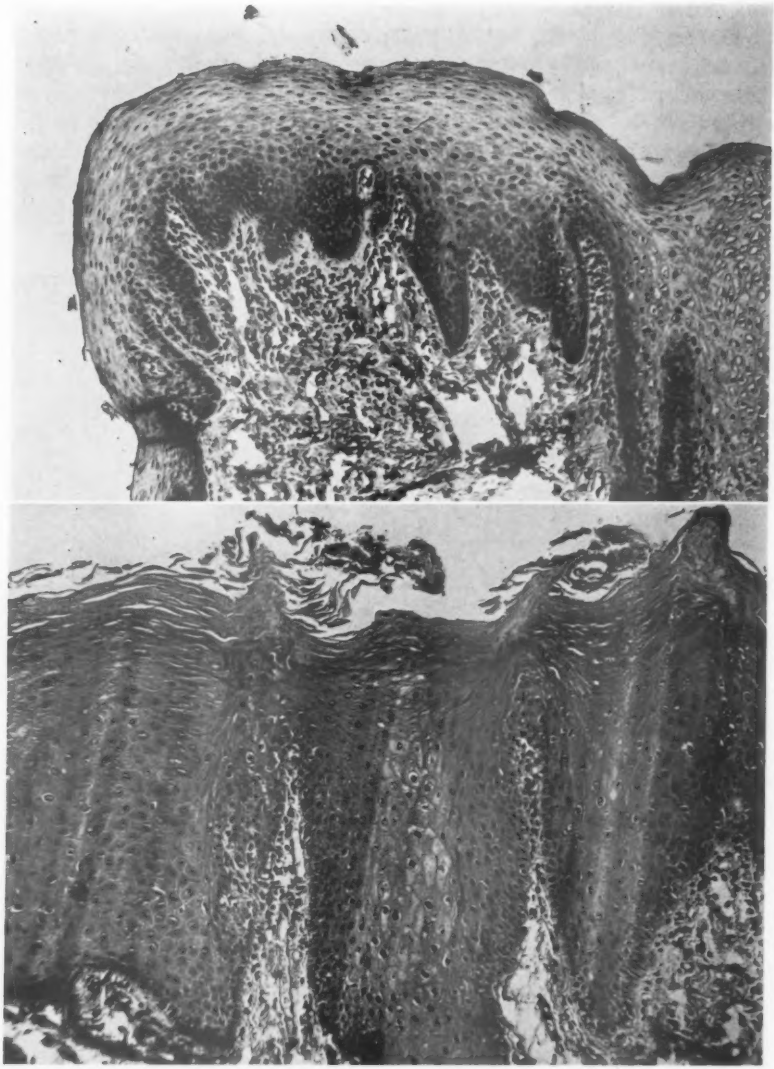
Fig. 2.—*A*, Mild glossitis in iron-deficiency anemia. Grossly, the papillae appeared to be absent. When viewed under a surgical microscope, however, they were found to be present but stunted.

B, The same tongue following iron therapy, with return of the mucosa to normal morphology.

C, Complete atrophy of the tongue in Plummer-Vinson syndrome.

D, Return to normal after therapy with iron.

A.



B.

Fig. 3.—*A*, Tongue biopsy specimen prior to therapy. Note the smooth nonparakeratotic surface with loss of filiform papillae and reduction in thickness of epithelium. (Hematoxylin and eosin stain. Magnification, ×170; reduced ¼.)

B, Posttreatment biopsy specimen of the tongue. Note return of filiform papillae, parakeratotic layer, and thicker epithelial layer. The central epithelial cells between the papillae are larger than those shown in *A*. (Hematoxylin and eosin stain. Magnification, ×170; reduced ¼.)

corners, reduction of the nuclear diameter, and an almost complete disappearance of nuclear abnormalities. In the pretreatment observations, 2 to 83 per cent of the exfoliated cells were of the cornified epithelial type, 15 to 98 per cent were precornified, and 0 to 10 per cent were keratinized. Following iron therapy, the cytoplasm to nucleus ratio of the majority of these cells returned to normal.

When the appearance of the individual population of cell types (for example, cornified and precornified) was qualitatively and quantitatively evaluated before and after treatment, it was found that each group exhibited the abnormalities already described in the individual cells before treatment with a change toward the normal after treatment. Evidence of improvement in the exfoliated cells was apparent within one to two weeks after iron therapy.

On gross inspection of the tongue mucosa before therapy, there appeared to be complete disappearance of the papillae of the tongue in most instances. Atrophy was more severe at the margins and tip of the tongue, and occasional patches of atrophic mucosa were irregularly spread over the dorsum of the anterior third. When viewed under the surgical microscope, areas of apparent complete atrophy showed flattened fungiform and filiform papillae (Fig. 2).

A pretreatment histologic section of the mucosa of the tongue is shown in Fig. 3, *A*. The specimens consisted of mucosa and underlying connective tissue and skeletal muscle. Absence of papillae or diminution in the size of the papillae and thinning of the parakeratotic epithelial layer were noted. The nuclei of the cells of the epithelium were enlarged, but the over-all cell size was less than in the normal control and posttreatment patients. Less periodic acid Schiff-positive diastase-digested material was present in the cytoplasm than in posttreatment and normal control sections of the tongue. A questionable increase in cytoplasmic epithelial pyroninophilia, as detected by the methyl green-pyronine stain, was also noted in the untreated cases. In two months after treatment, the structure returned to normal (Fig. 3, *B*).

DISCUSSION

It is well known that a severe iron-deficiency anemia may occur without evidence of glossitis or atrophy of the lingual mucosa. However, when these symptoms and signs are present in a patient with a microcytic-hypochromic anemia, it is commonly accepted that they are related to iron deficiency. Severe glossitis may appear in patients with iron-deficiency or pernicious anemia in spite of adequate food intake and supplemental vitamins.[4] Similar observations have been made in pernicious anemia in which approximately 50 per cent of the patients demonstrate symptomatic or morphologic alterations of the tongue.[5] These clinical facts raise the question of the specificity of iron deficiency as the sole etiological factor in the pathogenesis of this lesion. Seldom, in clinical medicine, do we encounter a deficiency state of single cause. The symptoms of glossitis and atrophy of the tongue are encountered in most persons suffering from anemia for many months or several years. Superficial gastritis, atrophic gastritis, and gastric atrophy are frequently encountered in patients with iron-deficiency anemia.[6] That the lesion of the gastric mucosa precedes and favors

the anemia and is not improved by its correction is a common belief.[7] In some of these patients dietary inadequacy is suspected. A faulty diet may result from the chronic disease state, augmented by anorexia and exaggerated by the appearance of glossitis which, in turn, interferes with normal dietary habits. Further dietary restrictions are encountered in those persons who subsequently develop a dysphagia (Plummer-Vinson syndrome). An adequate evaluation of food intake, both qualitative and quantitative, was impossible for our patients, but there appeared to be distinctly unsatisfactory dietary habits in only two of five patients. If inadequate diet (lack of vitamin B complex other than B_{12} and iron) is the major etiological factor in the glossitis of pernicious anemia and iron deficiency, a similar cytologic lesion of the tongue could be expected. In pernicious anemia and sprue[8-10] the cytoplasmic diameter of exfoliated cells may be tremendously enlarged, while in iron deficiency the cytoplasmic diameter is less than normal.

During the period of iron therapy, the patients received the average hospital diet; later, as outpatients, they were advised about an adequate diet. Iron-deficiency anemia with glossitis can be treated successfully by diet alone (hyperalimentation).[11] Beutler[12] has indicated that iron deficiency is manifest not only in anemia but also in the reduction of the systemic enzyme cytochrome which is concerned with respiratory function at a cellular level. Waldenström has ascribed the changes in the oral and esophageal mucosae also to the lack of the Warburg or cytochrome enzyme.[13]

The cytologic alteration of the lingual squamous mucous membrane cells in this study would suggest a maturation cellular defect with interference of RNA and DNA synthesis. Current investigation utilizing acridine orange with fluorescent microscopy is under way to evaluate this hypothesis on a cytochemical basis. The microscopic appearance of exfoliated epithelial cells in these observations is reminiscent of the cells that we have seen from patients with malignant disease. The giant nuclei, the bizarre shapes and forms, and the alteration of chromatin pattern by nucleation are all signs of cellular immaturity and could be classified as evidence of malignancy by the usual Papanicolaou criteria.

Symptoms and signs in relation to the oral mucosa are not infrequently observed in patients undergoing chemotherapy for systemic malignancy. Patients receiving folic acid antagonists, antipurines, alkylating agents, and anticonvulsants have demonstrated alteration in the exfoliated cells of the squamous epithelium of the mouth. These changes, hypertrophy of the cytoplasm and nucleus with thinning of the chromatin pattern, cytoplasmic vacuolization, and binucleation,[14, 15] suggest that the morphologic picture is related to alteration of nucleic acid metabolism.

SUMMARY AND CONCLUSIONS

The normal exfoliative cytology of the tongue is described. Five patients with moderately severe classic iron-deficiency anemia were studied in relation to the gross and microscopic appearance of the tongue, exfoliative cytology, and histology of the lingual mucosa before, during, and after therapy. In some

patients with apparent complete atrophy of the mucous membrane of the tongue, microscopic examination disclosed stunted papillae. Atrophy of the filiform papilla precedes that of the fungiform papilla. After iron therapy there is restoration toward a normal state. Exfoliated squamous epithelial cells of the tongue in cases of severe iron deficiency demonstrated a marked deficiency in the cornified and keratinized population. The cytoplasmic diameter of exfoliated cells was reduced with paradoxical enlargement of the nucleus. The nuclear pattern was altered, and abnormal cellular maturation was found, as evidenced by a disturbed nuclear pattern, an increase in nucleoli, the presence of double nuclei, and karyorrhexis. Histologic sectioning of the tongue in patients with iron deficiency and glossitis demonstrated atrophy or absence of papillary formation, lack of keratinization, and thinning of the mucosa. After a course of iron therapy and adequate diet, the cytologic and histologic appearance as well as the gross structure returned to normal. Iron, rather than vitamins of the B complex, is believed to be the major factor in the production of lingual lesions in an iron-deficiency state. To substantiate this impression, a study of intensive intravenous treatment with vitamin B compounds prior to iron administration is planned.* Iron-deficiency anemia is a systemic disease in which oral manifestations are important and re-emphasize the role of iron in body metabolism at a cellular level.

Our findings suggest the usefulness of the techniques described in the diagnosis and management of deficiency states. The methods may be of value in the diagnosis of oral lesions of unknown etiology and pathophysiology. The in vivo metabolic effects of therapeutic agents on the morphology of exfoliative cells of the oral cavity may prove to be a rewarding investigational tool.

The authors are most grateful to Mrs. Elizabeth Watson for valuable assistance in the preparation and interpretation of the Papanicolaou preparations and to Dr. Marvin Revzin and associates for obtaining the surgical biopsy specimens of the tongue.

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RUDOLPH VIRCHOW: PATHOLOGIST, ANTHROPOLOGIST, AND STATESMAN*

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WHEN Rudolph Virchow died, it was said that Germany lost not only its leading physician but also its leading anthropologist, sanitarian, and liberal politician. In this presentation, I shall attempt to present a brief résumé of the life of this man who has been called the father of modern pathology.

Virchow was born in 1821 in the German province of Pomerania. His parents were of lower middle class extraction, and he was an only child. It is interesting to note that Virchow was born at about the same time as many others who were to play leading roles in the years to come. For example, Helmholtz, Mary Baker Eddy, and Gustave Flaubert were born in the same year as Virchow. Claude Bernard, Semmelweiss, Queen Victoria, Karl Marx, Walt Whitman, Melville, Pasteur, Mendel, and Lord Kelvin were all born within a few years of Virchow's birth.

In 1839 Virchow entered the Friedrich Wilhelm Institute, one of the two prominent medical schools of Prussia. Among the members of the teaching staff at the Institute were Johannes Müller and Schönlein; Virchow's classmates included Helmholtz and DuBois-Reymond. Upon graduation from the Institute, where his record had been quite notable, Virchow became assistant to Robert Frorieps, the prosector at the Charité Hospital in Berlin.

This is an excellent point at which to change our reflection and to review the medical accomplishments of Virchow, since his most active period of work in medicine was in the early years of his life.

In 1844, Frorieps requested that Virchow investigate Cruveilhier's concept of phlebitis as a basis of inflammation and also asked him to investigate the relation of coagulation to inflammation. After extensive animal experimentation and numerous necropsy observations, Virchow defined the concepts of thrombosis, embolism, and the relationship of fibrin to the clotting mechanism; formerly, hypinosis and hyperinosis had been designated as types of constitutions to explain the clotting mechanism. While working on this project,

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Virchow noted that the blood settled more rapidly in tuberculous patients than in normal persons and proposed a test which we take for granted today—the sedimentation rate. Also in 1845, while performing a necropsy on the body of a woman with splenomegaly and a bleeding tendency, Virchow noticed that the blood was pale red. Following this experience, he accurately described the condition which we know today as leukemia; at that time he called it *weisses blut*. In the same year Craigie and Bennett also described the condition; they thought that it was a pyemia. Virchow believed that pus cells could not pass through the walls of blood vessels and therefore suggested that the condition was not pyemia but a particular disease process caused by the spleen. Later, his pupil, Conheim, showed that Virchow's reasoning was faulty but his conclusion correct. It is interesting to note that there ensued in the medical journals of the day a lively debate between Virchow and Bennett for priority in the discovery of leukemia.

In 1846 Frorieps resigned as prosector at the Charité Hospital, and Virchow was appointed to the post. In the following year, associated with Bruno Reinhardt, Virchow established the *Archives of Pathology and Clinical Medicine*. At that time many new medical journals were being published in Germany, much as in our country today. However, the *Archives of Pathology and Clinical Medicine*, by virtue of its strict editorial policy and excellent articles, soon rose to the top. After Reinhardt's premature death in 1852, the journal became known as *Virchow's Archives*.

In 1846, Virchow began work on a textbook related to Rokitansky's theory of crasias and dyscrasias. This theory, which may be difficult to grasp in the light of our present-day knowledge, maintained that when findings at necropsy did not sufficiently explain the patient's symptoms, the symptoms were due to an anomalous condition in the blood; in other words, this was a concept of humoral pathology similar to that advanced by Galen. We must bear in mind that at this time Virchow was a young man, only 25 years of age, and a recent graduate from medical school, while Rokitansky was a leading pathologist in Europe. Virchow had Johannes Müller's support, however, and he also had a well-founded theory of diseases based on scientific facts and common sense. Virchow countered Rokitansky's humoral theories with the concept of "cellular pathology" which was embodied in his creed: *Omnia cellula e cellula.*

As precursors of Virchow's concept of cellular pathology, it is noteworthy that in 1839 Schwann advanced the cell theory, that is, the theory that all animal matter was composed of small units called cells. This was a companion theory to that which Schleiden advanced for plant life. Most authorities, however, including Schwann, believed that the cells arose from a fluid blastema; in other words, they believed in the spontaneous generation of cells. Through the cellular theory, Virchow suggested that connective tissue was cellular rather than acellular and that intramembranous and enchondral ossification occurred. Likewise, through the cell theory, he suggested that neoplasms were local rather than constitutional entities. It is interesting to note that Virchow had misconceptions concerning the metastases of neoplasms and the origin of cancer. He

believed that metastases occurred when a fluid released by the cancer stimulated cells in an organ to proliferate and he thought that most cancers arose in connective tissue. Virchow removed tuberculosis from the realm of the dyscrasias; formerly, granulomas like those present in tuberculosis were thought to be collections of cells arising from an acellular blastema as part of a humoral tendency. If we explore this point further, however, we realize that Virchow did not recognize tuberculosis for what it was. Instead, he believed that caseous granulomas represented a type of degenerative change which could be seen in cancer, typhoid fever, glanders, and other conditions; in other words, tuberculosis was not a specific condition. On the other hand, he thought that in the lung, tubercles were a complication of phthisis which, in turn, was believed to be a type of chronic penumonia.

In 1848 Virchow was dismissed from the Charité Hospital because of his revolutionary political activities, but he was given the professorship in pathology at Würzburg. In the same year he married the daughter of a prominent obstetrician in Berlin. Virchow's stay at Würzburg was productive; he elucidated his work on thrombosis and embolism, defining bland and septic emboli. Also, he wrote a handbook of special pathology which described necropsy techniques and defined amyloidosis. Prior to this, the Vienna School had described the lardaceous spleen and liver. Virchow demonstrated the iodine and sulfuric acid reaction in lardaceous and sago spleens, as well as in kidneys, and coined the term *amyloid*. He also discovered corpora amylacea in the brain, which also stained blue with iodine.

In 1856, after an absence of several years, he returned to Berlin as a professor at the new Institute of Pathology. It is of interest that at 35 years of age, through his investigations, his books, the *Archives*, and his presentation of cellular pathology, Virchow was considered to be among the immortals of medicine. In 1858 the first edition of his celebrated book, *Cellular Pathology*, was published. In the same year as this eventful publication Virchow's professor, Johannes Müller died. Elsewhere in the world that eventful year Queen Victoria married Prince Albert, Livingston sailed for Africa for the first time, Darwin presented his findings to the Linnaean Society, Mark Twain was piloting a Mississippi steamer, and Dickens was writing *A Tale of Two Cities*.

During the remainder of Virchow's life he made few more original contributions to anatomic pathology. Perhaps this was because he had become interested in anthropology. One of his other contributions was a lengthy treatise on trichinosis, published in 1854, in which he elucidated the nature and transmission of the disease as well as prophylactic measures to be used in combating it.

During the later years of his life Virchow proved somewhat resistant to the new findings in bacteriology as explanations for infectious disease. Perhaps this was a result of overcautiousness. At any rate, there ensued a debate with Klebs and Koch over the true significance of the tubercle bacillus.

In 1888, Virchow performed his last necropsy, which was upon the body of Emperor Frederick III. This interesting case has provoked much discussion

during the ensuing years. As you probably know, Frederick III is said to have died of laryngeal carcinoma. When hoarseness was first noted, two German physicians believed that the condition was malignant and suggested that a laryngectomy should be performed. However, Frederick's English wife was terrified at the thought of her husband undergoing a radical operation and consulted her aunt, Queen Victoria. Queen Victoria sent the English laryngologist, Mackenzie, to Germany to examine Frederick. Mackenzie differed with the Germans and biopsied the tumor, which was interpreted by Virchow as being a benign lesion. In the next two months two more biopsies by Mackenzie were also interpreted as benign. In defense of Virchow, however, it must be pointed out that Mackenzie had apparently removed overlying inflammatory tissue which did not include the neoplastic tissue.

His work in pathology was only one part of Virchow's medical accomplishments. He was one of the major contributors to progress in public health and in 1848 investigated a typhus epidemic in Silesia, concluding that the spread of the disease was due largely to famine and poor housing. He concluded that the epidemic would not have occurred if the people had been free, educated, and prosperous. This was the first outward manifestation of Virchow's liberal tendencies. In 1848 and 1849 he investigated a cholera epidemic and again reported the social implications of the condition. He constantly advocated improvement of social conditions as prophylaxis against epidemics.

It is difficult to separate Virchow's public health ideas from his sociopolitical ones. He advocated shorter working hours, a decrease in unemployment, insurance for invalids, and free medical care for the indigent. From 1862 through 1872 he was concerned with improving the Berlin sewage disposal system. Through his influence, cesspools and wells were abolished and the use of the Spree River as an outlet was discontinued.

As a sidelight, during the war of the 1860's and 1870's he recognized and improved the poor sanitation in the military barracks. Also, he instigated the opening of the first nursing school in Berlin. As a result of Virchow's urging and the efforts of other liberals of the day, Germany instituted one of the first systems of compulsory health insurance.

As you may have ascertained, Virchow was politically oriented and an avowed liberal; even in his student days, he participated in organizations which opposed the semifeudal order of the German States. His report on the epidemic in Upper Silesia was a major contribution to the revolt of 1848, although he was in the barricades of Berlin during the revolt. As a result of this short-lived and unsuccessful revolt, Virchow lost his position at the Charité Hospital in Berlin. Perhaps it was because its leaders were teachers, businessmen, and philosophers rather than soldiers that the revolt failed. Virchow's thinking at this time may be summed up in a quotation attributed to him; in referring to the kings of Prussia, he said: "I know of a family, a very exalted one, in which the grandfather had softening of the brain, the son hardening of the brain, and the grandson no brain at all." It is interesting that another liberal, Karl Marx, also played a secondary role in this revolt and, upon its failure, went into exile in England.

Virchow's goal was the unification of Germany into a republic, with abolition of the many states and with self-government. He clearly recognized the autocracy of the Hohenzollerns.

His other goal was to improve the lot of the working man. In 1857 he was elected to the Prussian Parliament and immediately became a leader in fighting the laws that favored the Junkers. As the liberals seemed to be making headway in the fight, in 1862 the kaiser appointed a new prime minister, Otto von Bismarck. From the first, Bismarck was obsessed with the idea of German unification through "blood and iron," with Prussia rather than Austria in the position of leadership. This was done by provoking Austria into war, partially over the Schleswig-Holstein issue; the war culminated in a Prussian victory at the Battle of Sadowa in 1866. Throughout, Virchow opposed Bismarck's Junker and almost dictatorial actions. In 1865 one of these criticisms was interpreted by Bismarck as an aspersion on his truthfulness. At this point he challenged Virchow to a duel; Virchow refused, saying that his life was far too valuable to mankind to be risked in a duel with a politician. Shortly after this incident, Virchow appears to have been fooled by anti-French propaganda. His writings were markedly anti-French and he advocated the superiority of German medicine. Shortly before the outbreak of the Franco-Prussian War, however, he realized his errors and publicly rescinded his statements. He was violently against the war and was roundly criticized for his attitude.

In the 1880's he was firmly opposed to Bismarck's policy of colonial expansion in Africa. Also, in 1880, Bismarck tried to bring the laboring masses more into line by supporting an organization known as the Christian-Social Party which had anti-Semitism as its basis. Stoecker was the leader of this group and was a candidate in the 1880 elections. Virchow was a candidate against Stoecker and his party and defeated them.

In summary, Virchow's political career was one of firm opposition, which was largely unsuccessful. Perhaps it was unsuccessful because of the German people's tradition of submission to the Hohenzollerns and Junkers.

Virchow was so prominent in anthropologic circles that one anthropologist was said to have wondered if the famous anthropologist was related to the doctor of the same name.

One of Virchow's first projects in the early 1850's was a lengthy work on the sizes and shapes of skulls. Much of this material is used by anthropologists today.

Virchow accepted the theories of evolution only with reservation. For example, he opposed the idea of the Neanderthal man, believing that it was a recent specimen with hyperostosis, rickets, and Paget's disease. Likewise, he refuted *Pithecanthropus erectus*, claiming that it had the skull of a type of gibbon. With this negative approach, Virchow is said to have retarded the progress of German paleontology.

In 1871 a French author claimed that German unity was due to an anthropologic error and that Prussians were racially Finns and differed from the Germans, who were a blond group. As a result, Virchow began an extended study of Finnish, Prussian, and German skulls. Also, he made a monumental survey

of the color of hair, eyes, and skin of 6,700,000 German schoolchildren; he divided them into religious groups and concluded that nowhere were Germans uniform and that certainly they were not predominantly blond. He also noted the same percentage of blonds in the Jewish and in the non-Jewish children; anti-Semites never forgave him for this objective treatment of the problem. Of Virchow's 1,180 articles on anthropology, over 500 dealt with archeology. His first discovery was a group of piled dwellings in North Germany in 1865. In 1875 he and Robert Koch embarked on a similar excavation in Pomerania in an investigation of Bronze Age grave fields. In the late 1870's he became interested in Near East archeology. Joining Schliemann, who had excavated the cities of Troy, he spent several summers excavating in Troy, Micenia, and Egypt. Finally, in 1895, Virchow pioneered in the use of the x-ray in archeology.

It is really amazing that Rudolph Virchow was simultaneously engrossed in all the subjects mentioned, went into them as an active participant, and explored them well. It is also of interest that he was favored by excellent health. He was never seriously ill prior to the age of 81 years, and he usually slept only four to five hours a night. He was assisted greatly by the recent development of the improved microscope. Also, the early deaths of Meckel, Reinhardt, and Remak helped make it possible for him to assume a role of great stature in German medicine so rapidly. Despite this, Virchow was an extraordinary person who belongs not only to pathology and medicine but to all of the physical and political sciences.

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ORAL PATHOLOGY

General Section

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BONE SARCOMA

Report of an Interesting Case

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THE increasing use of irradiation for therapeutic purposes has produced an apparent rise in the incidence of bone sarcoma.[6, 8, 9] Although postradiation bone sarcoma currently appears to be relatively rare, its presence in the jaws is notable since bone sarcoma in this location is unusual.

The occurrence of sarcoma in bones other than the jaw which had been irradiated and which had exhibited no prior lesion is less than 50 per cent. Tanner and associates[3] report four cases of sarcoma complicating fibrous dysplasia following irradiation. In all four instances, the facial bones were the only ones involved by fibrous dysplasia. To date, so far as is known, these are the only reported cases in which bone sarcoma involving the jaws might be attributed to radiation. The article by Tanner and his colleagues contains an excellent review of the literature concerning this problem.

The following case exhibits some similarity to those reported by Tanner and associates.

CASE REPORT

In February, 1949, a 51-year-old white woman who complained of a swelling of the right mandible was seen by one of us (K. H. T.) for the first time. The referring dentist reported that when he first saw the patient she had complained of a recurrent, painless swelling with discharge in the lower right molar region which had been present for three

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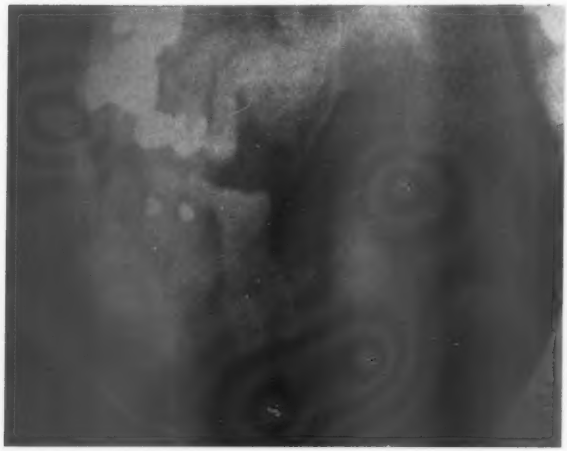


Fig. 1.—Roentgenogram of right side of mandible taken in 1949.

years. A biopsy report at that time indicated ossifying fibroma. Approximately two months later, a second biopsy specimen from the body of the mandible on the right side was reported as indicative of Paget's disease.

Examination revealed that the mandible on the right side, which was edentulous, was slightly expanded. There was no pain, and palpation revealed no tenderness. The blood chemistry was essentially normal, as follows: calcium, 10.07 mg. per cent; phosphorus, 2.5 mg. per cent; and alkaline phosphatase, 6.3 King-Armstrong units. Roentgenograms showed bilateral areas in the mandible which were radiolucent but which contained areas of irregular radiopacity (Fig. 1).

A clinical diagnosis of fibrous dysplasia was made. The mandibular teeth were extracted and tissue was taken for microscopic examination.

Pathologist's Report.—The specimen consisted, for the most part, of dense bone which exhibited on its periphery a cellular, collagenous connective tissue containing nodules and abortive trabeculae of bone (Fig. 2). In no instance did the bone, either central or peripheral, exhibit a normal architecture. The dense central portion was devoid of well-formed Haversian systems, but there was some evidence of lamellation. The bone was somewhat fibrillar and in one area it exhibited some rather coarse trabeculation. The over-all appearance in the trabeculated areas suggested an initial formation of nodules which subsequently had become confluent by the further deposition of bone. The lacunae were arranged in a haphazard fashion and were irregular in shape. Osteocytes were seen infrequently. On the periphery there was noted, as previously stated, collagenous connective tissue which exhibited a marked cellularity (Fig. 3). In some places in this tissue the formation of atypical bone remindful of reactive or osteophytic bone could be seen. In other areas the bone appeared as calcified nodules which varied in size and shape, took a blue stain, and exhibited a paucity of cells. In a few places both types of bone were seen within the same spicule. *Diagnosis:* Fibrous dysplasia.

Subsequent Course.—In March, 1949, radiation treatment was given at a local hospital. The patient received 1,440 r to each side of the mandible in six treatments.

In July, 1949, the patient was referred back to K. H. T. for treatment of a persistent fistula.

In January, 1950, a roentgenogram taken at a local hospital showed an increase in the size of the mandible. Lesions in the skull were found to be larger than in earlier roentgenograms; we were unable to obtain a report on the earlier roentgenograms.

Fig. 2.

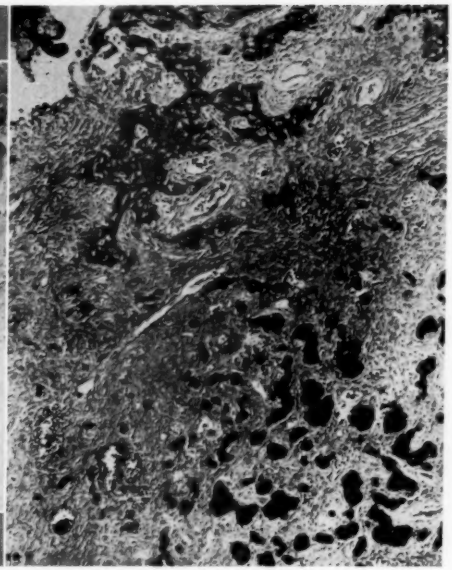
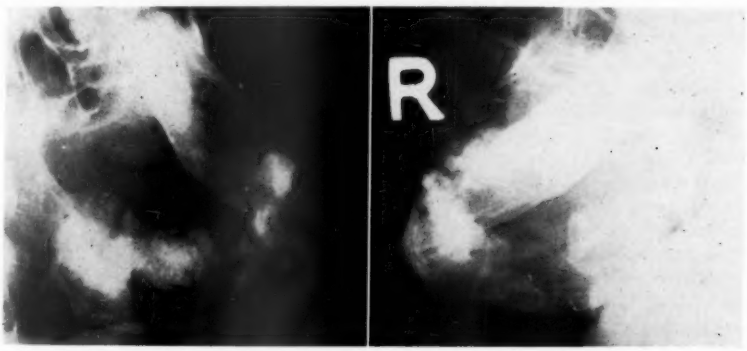


Fig. 3.

Fig. 2.—Photomicrograph of biopsy taken in 1949. Note fibrous area with calcifications. (Magnification, ×7.5.)

Fig. 3.—Fibrous area shown in Fig. 2. The characteristic pattern of fibrous dysplasia is evident. (Magnification, ×53.)



A. *B.*

Fig. 4.—Lateral jaw roentgenograms taken in 1958. *A*, Left side; *B*, right side with osteolytic area.

Four times during the ensuing year sequestra were removed by a local dentist. In April, 1954, a sequestrum was removed from the lower right third molar region. Another was removed in August, 1954, but the location was not indicated. A sequestrum was removed from the premolar area (side not indicated) in October, 1954, and in January, 1955, another sequestrum was removed and submitted for pathologic study. The pathologist returned a diagnosis of Paget's disease.

In June, 1955, a roentgenogram of the patient's swollen left knee was negative.

Fig. 5.—Roentgenogram of skull taken in 1958 showing evidence of Paget's disease.

In September, 1958, the patient consulted her local dentist because of pain in the right mandible. A biopsy specimen taken from the body of the mandible on the right side was reported to show osteogenic sarcoma.

The patient was referred again to K. H. T., who found the mandible on the right side to be swollen from the second premolar to the inferior border of the mandible. The mucosa was red and exhibited an ulceration in the area from which the biopsy specimen had been taken. X-ray examination revealed an osteolytic area in the molar region of the right mandible (Fig. 4). Roentgenograms of the entire skeleton revealed abnormalities in the skull only, which were diagnosed as Paget's disease (Fig. 5). Studies of the blood chemistry at this time revealed the calcium and phosphorus levels to be normal, but the alkaline phosphatase was 16 Bodansky units.

The right mandible, including the ascending ramus, was resected by Dr. Thoma. Slides were prepared from two parts of the gross specimen and examined.

Pathologist's Report.—Specimen No. 1 consisted of a roughly circular piece of bone, the architecture of which had been markedly altered. At the periphery, the pattern suggested cortical bone. However, the classic arrangement was seen to have been distorted by resorption and replacement by a dystrophic bone which exhibited a mosaic pattern such as that seen in Paget's disease (Fig. 6). Haversian systems were scarcely recognizable and occurred infrequently. There were no well-defined lamellations. The lacunae were irregularly arranged and were more oval than slitlike. Occasionally, there could be seen a thin residuum of the outer circumferential lamellae. Moderate to marked activity could be seen, with neither resorption nor apposition dominating. The medulla was so altered as to be unidentifiable as such. Here the bone, which was less dense than that on the periphery, exhibited the same characteristics. There were at least two areas in which groups of small unconnected spicules were seen. For the most part, the marrow was seen to be replaced by a markedly cellular, densely fibrous, connective tissue tumor (Fig. 7). What marrow remained appeared

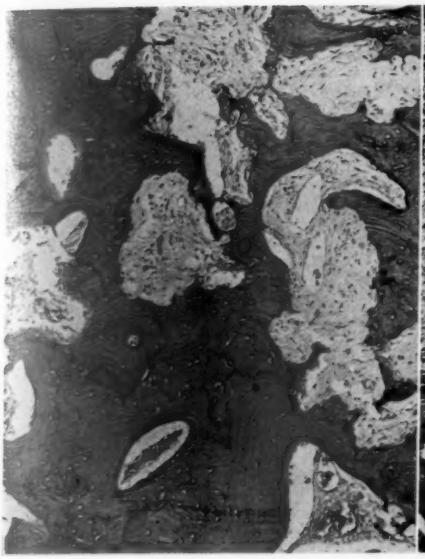


Fig. 6.

Fig. 7.

Fig. 6.—Photomicrograph of area from mandibular resection in 1958 exhibiting characteristics of Paget's disease. (Magnification, ×53.)

Fig. 7.—Photomicrograph of fibrosarcoma found in mandibular resection in 1958. (Magnification, ×53.)

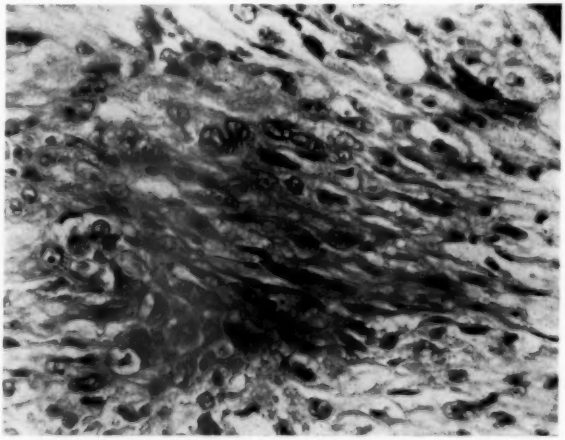


Fig. 8.—High-power photomicrograph of fibrosarcoma shown in Fig. 7. (Magnification, ×368.)

as a loose, fibrous, vascular, moderately cellular connective tissue. The cells of the tumor were identifiable as fibroblasts and exhibited considerable atypia, pleomorphism of nuclei, and numerous mitotic figures. Hyperchromatism of nuclei was common, and tumor giant cells were frequently seen (Fig. 8). The bone, although obviously abnormal, did not appear to be the product of the malignancy. *Diagnosis:* (1) Fibrosarcoma; (2) Paget's disease.

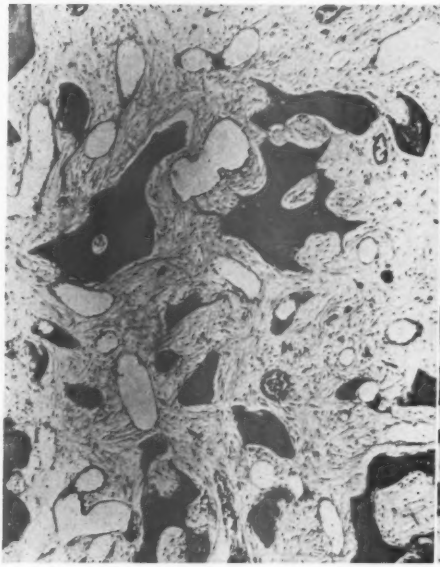


Fig. 9.

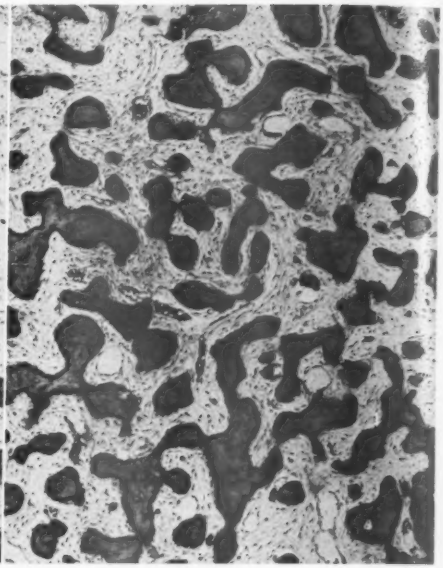


Fig. 10.

Fig. 9.—Photomicrograph of area from mandibular resection in 1958 exhibiting characteristics of fibrous dysplasia. (Magnification, ×53.)

Fig. 10.—Photomicrograph of area from mandibular resection in 1958 exhibiting characteristics of fibrous dysplasia with cementum-like formations. (Magnification, ×53.)

Specimen No. 2 consisted of a roughly triangular piece of bone which presented the same alterations as those seen in the first specimen, except that there were seen larger areas of the bone which occurred as spicules. This bone fell into two morphologic categories: (1) cellular bone which manifested a pink stain (Fig. 9) and (2) a relatively acellular material which

Fig. 11.—Photograph showing the rapidly growing tumor shortly before the patient's death.

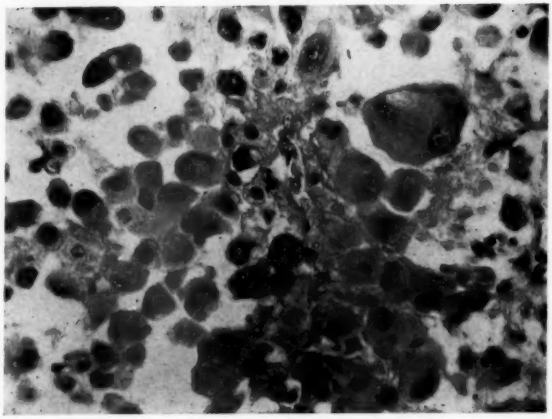


Fig. 12.—High-power photomicrograph of anaplastic tumor as seen in final biopsy. The change from the condition shown in Fig. 10 is striking. (Magnification, ×318.)

took a blue stain and resembled cementum (Fig. 10). In some areas these two types of bone were intermingled. Again, one is impressed by the fact that the bone was not being formed as a part of the malignancy. In this instance, there was little evidence of changes consistent with Paget's disease. Instead, there were changes fully consistent with fibrous dysplasia. The tumor was invading the atypical bone. *Diagnosis:* (1) fibrosarcoma; (2) fibrous dysplasia.

Postoperative Course.—During the third postoperative week, the patient developed an extensive swelling of the right cheek which resembled a cellulitis. Then, two days later, the patient exhibited several carbuncle-like lesions on the cheek (Fig. 11) and was readmitted to the hospital. An intraoral biopsy specimen and cultures from an attempted incision and drainage of the carbuncle-like areas were taken. The cultures were negative. The pathologic findings were those of an undifferentiated fibrosarcoma. This tumor was characterized by a marked anaplasia, pleomorphism, and numerous tumor giant cells (Fig. 12). Shortly thereafter, the patient died.

DISCUSSION

It would be most interesting if the course of events were fibrous dysplasia—irradiation—sarcoma. This may very well have been the case. However, the probable presence of Paget's disease suggests the sequence of Paget's disease followed by sarcoma of bone. It is known that a number of bone diseases may exhibit microscopic characteristics of other diseases, particularly at the periphery; even so, in the case just reported there were indisputable microscopic changes which were clearly compatible with a diagnosis of fibrous dysplasia on the one hand and Paget's disease on the other.

The normal serum phosphatase in 1949 was more consistent with fibrous dysplasia than with Paget's disease. This was also true of the x-ray changes seen in the mandible. Yet, fibrous dysplasia usually manifests itself in early childhood or adolescence; this patient was 51 years old at first presentation. The patient's age, the skull roentgenograms, and the interpretation of some of

the biopsy specimens are consistent with Paget's disease, but the normal alkaline phosphatase in 1949 is not consistent. The elevated phosphatase level reported in 1958 could be attributed to the sarcoma. It would have been helpful to repeat these tests.

The weight of the evidence favors the probability that the patient suffered originally from Paget's disease which was subsequently complicated by sarcoma of bone. However, it is tempting to consider the concomitant existence of Paget's disease and fibrous dysplasia, a combination which to our knowledge has never been reported. The relationship of the terminal sarcoma to the radiation received by the patient is obscured by the fact that Paget's disease is known to be complicated by sarcoma in an estimated 10 per cent of the cases.[1] Nevertheless, the amount of radiation given to the patient has been thought to be sufficient to induce sarcoma.[8] The interval of nine years between the x-ray treatments and the appearance of the tumor is consistent with the estimated latent period.[8] Although it is unlikely that in this case the diagnosis can be properly considered to be other than Paget's disease complicated by sarcoma, it is possible that, as additional information concerning the relationship of irradiation and malignancies of the jaws becomes available, the events recorded in this report may be subject to reinterpretation.

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SECONDARY NEUROBLASTOMA OF THE MANDIBLE

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IT IS rare for a neuroblastoma to present as a swelling of the mandible. Therefore, the following case is of interest.

CASE REPORT

Clinical Findings.—A 2½-year-old boy appeared slightly unwell and tired easily. He was irritable and complained of abdominal discomfort. After two weeks a small swelling was noticed on the lower right gingiva.

This swelling, which increased rapidly in size during the next two weeks, was thought to be an alveolar abscess. Because of this, the boy was referred to The London Hospital's dental department where he was admitted and examined under general anesthesia. The lower central deciduous incisors and the lower right lateral deciduous incisor and canine were found to be very loose and were removed with adjacent soft tissue of the swelling for biopsy. There was a large abdominal mass in the epigastrium, to which no edge could be felt. The mass was firmly fixed to the posterior abdominal wall and did not move with respiration. Radiographs of the jaw showed bone loss in relation to the elevated and separated teeth (Fig. 2). Nothing abnormal was detected in radiographs of the chest, abdomen, and skull.

Histologic Findings.—Examination of the biopsy specimen revealed a tumor consisting of closely packed, small, round cells with deeply staining nuclei and very little cytoplasm (Fig. 3). Distribution of the cells was devoid of pattern, and none of the characteristics of early differentiation of neuroblasts were found. Sections of the lateral incisor showed an intimate relationship between the tumor mass and the root surface, with complete destruction of the alveolar process and periodontal membrane (Fig. 4).

Progress.—A course of deep x-ray therapy to the growth in the mandible produced a considerable regression with local improvement, but it was thought that irradiation of the abdomen would not be justifiable. In the two weeks following the child's admission to the hospital, the abdominal mass increased in size, with great abdominal distention, dilatation of the umbilical veins, progressive anemia, and wasting. The patient died peacefully twenty-five days after admission.

Postmortem examination (by Dr. K. Weinbren) disclosed a partly necrotic and grossly hemorrhagic tumor of the right adrenal gland which measured 11 by 7 by 6 cm. A mass of diffuse growth (approximately 10 by 10 cm.) extended into the retrorenal and retroperitoneal tissues, completely surrounding the aorta and inferior vena cava. This diffuse growth was adherent to the undersurface of the liver, transverse colon, stomach, and left adrenal gland and had completely obliterated the pancreas. The tumor had penetrated into the right renal vein and inferior vena cava, and there were isolated secondary deposits in the liver and the falciform ligament in addition to that in the mandible.

From the Department of Dental Pathology, The London Hospital Medical College, University of London.

This case was first reported to the Section of Odontology of the Royal Society of Medicine on April 28, 1958.

For the most part, microscopic examination of the primary growth showed a picture similar to that of the secondary deposit in the jaw. In some areas, however, there were groups of cells with larger nuclei having a more open chromatin network and well-defined nucleoli (Fig. 5).

COMMENT

Neuroblastomas are rare, highly malignant tumors consisting of immature undifferentiated neuroblasts derived from the embryonic neural tube and neural

Fig. 1.

Fig. 2.

Fig. 1.—Lingual and buccal swelling of the alveolar process and separation of teeth in the region of the lower right incisors and canine.

Fig. 2.—Intraoral radiograph showing bone loss in relation to the lower right incisors and canine.

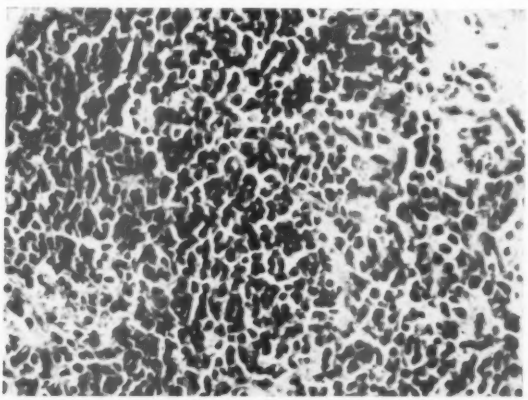

Fig. 3.—Section of biopsy from swelling of mandible. (Hematoxylin and eosin stain. Magnification, ×300; reduced ⅓.)

Fig. 4.—Section of the lower right lateral incisor with darkly stained mass of secondary deposit on labial surface of root. (Hematoxylin and eosin stain. Magnification, ×10; reduced ⅕.)

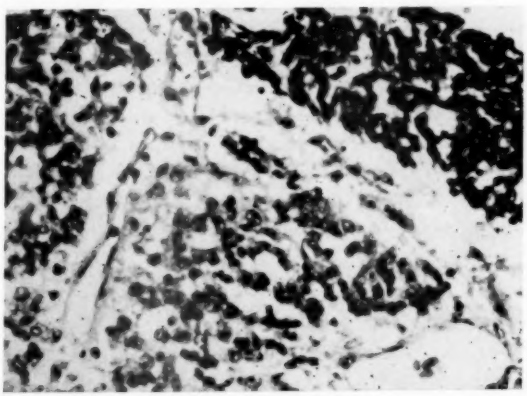

Fig. 5.—Section from the primary growth replacing the right suprarenal gland, showing areas of larger cells with nuclei having a more open chromatin network and well-defined nucleoi. (Hematoxylin and eosin stain. Magnification, ×300; reduced ⅕.)

crests. The great majority arise from the adrenal medulla or the sympathetic ganglia, particularly the large sympathetic ganglia in close proximity to the adrenal glands. They are virtually unknown in the central nervous system. They occur almost exclusively in infancy or early childhood, and surveys of the reported cases show that about 75 per cent of these tumors occur before the age of 4 years.[5] Neuroblastomas account for a high proportion of malignant tumors in this age group and are surpassed in frequency only by the renal embryonic tumors. Two patterns of metastatic spread have been described. The Pepper type consists of early extensive metastasis to the liver. In the Hutchinson type there is spread to the skull, dura, long bones, and sometimes the lungs. Secondary deposits in the skull are most frequently found in the calvarium, the base of the skull, and the retro-orbital tissues. The distribution of metastases from neuroblastomas does not follow one or the other of these two patterns as closely as was at first thought, and the present case is certainly not representative of either pattern.

Metastatic deposits involving the lower jaw are rare, only three established cases having been discovered in the dental literature. Burch[2] described the case of a 4-year-old boy whose right lower jaw was involved one week after the child's admission for investigation of an abdominal mass associated with loss of weight, vomiting, and pain. Cases in which a swelling related to the lower jaw has been a presenting symptom have been reported by Burford[3] and Blum.[1] The present case, in common with that reported by Blum, presented with symptoms simulating an inflammatory lesion. Histologically, neuroblastomas consist of closely packed sheets of small rounded or polyhedral cells with scanty cytoplasm and densely staining spherical or slightly ovoid nuclei. Mitotic figures are plentiful. There is usually very little stroma, and hemorrhage and necrosis are common. Many of these tumors are so undifferentiated as to be relatively indistinguishable from round-cell sarcomas, and many of the earlier reported neuroblastomas were thus described. Less rapidly growing neuroblastomas show early stages of neuroblast differentiation characterized by the appearance of tail-like cell processes, young nerve fibers, or the "rosette" grouping of cells. This rosette characteristic is probably a far less common feature of neuroblastomas than was once thought, and Stowens[4] found rosettes in only 15 per cent of his series of 110 cases. The absence of rosettes in the present case is consistent with the rapidity of the clinical course. The primary growths of neuroblastomas often show a higher degree of differentiation than the metastases. In the present case the groups of cells with larger nuclei, open chromatin network, and well-defined nucleoli found in the primary lesion appear to represent an early stage of differentiation not present in the secondary deposits.

SUMMARY

A secondary neuroblastoma in the mandible of a 2½-year-old boy is reported. The presenting feature was a swelling of the jaw simulating an acute alveolar abscess.

I wish to express my thanks to Mr. G. T. Hankey for permission to report this case and to Mr. A. J. King and Mr. A. L. Gallup for the photomicrographs.

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SUBMAXILLARY DUCT OBSTRUCTION FROM INVADING CARCINOMA

Report of a Case

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A male patient was first seen in the outpatient dental clinic. His chief complaint was a painful swelling in the left submaxillary region. Further questioning revealed that for a few months he had experienced some difficulty in swallowing. The painful submaxillary swelling was a new problem, however, with greater discomfort, and he sought aid for this reason.

Examination Findings.—There was a firm but not stone-hard swelling of the submaxillary gland. Cervical lymph nodes were not palpable. Intraorally, the tongue deviated to the left when protruded. When the tongue was reflected, the left floor of the mouth and the lower portion of the anterior pillar of the fauces were seen to be granulomatous and ulcerated, giving the clinical impression of carcinoma (Fig. 1). The floor of the mouth and the left posterior region of the tongue were hard and fixed. Lateral jaw films did not show invasion of the mandible.

Fig. 1.—Clinical appearance of squamous-cell carcinoma, visualized by reflecting the tongue.

No saliva could be milked from the left submaxillary duct. A sialogram and a biopsy were performed.

Histologic Study.—The tissue showed a keratinized stratified squamous epithelium beneath which there was invasion by a tumor composed of large anaplastic and hyperchromatic

cells showing nonuniform sizes, shapes, and staining qualities, lack of polarity, and occasional mitotic figures (Figs. 2 and 3). The diagnosis was Grade 3 squamous-cell carcinoma.

The sialogram showed a marked, tortuous constriction at the turn (comma) of the submaxillary duct. The portion of the duct anterior to the constriction was dilated from the

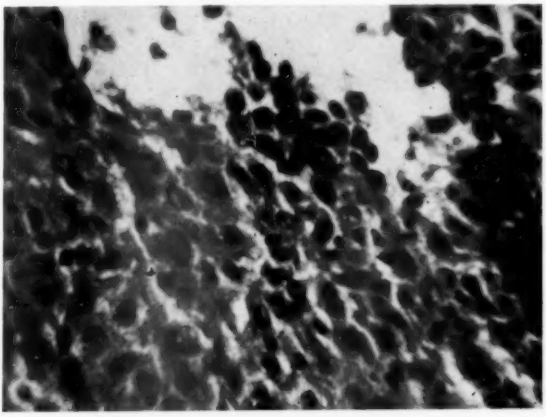

Fig. 2.—High-power photomicrograph of center of tumor, showing disproportion in sizes, shapes, and staining properties of cancer cells.

direct pressure of the contrast medium. The main duct of the gland itself was dilated and showed alternate constrictions and sausagelike dilations. The minor ducts were slightly dilated. The dye also found its way into the soft tissue posteriorly from the uppermost secondary duct which was invaded by the carcinoma (Fig. 4).

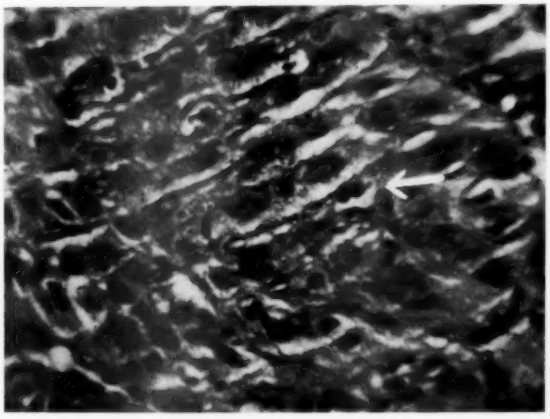

Fig. 3.—Photomicrograph showing the same characteristics as those shown in Fig. 2. Arrow points to atypical mitosis.

The patient was referred to the tumor clinic. For personal reasons, he went to a government hospital where he was receiving intra-arterial chemotherapy.

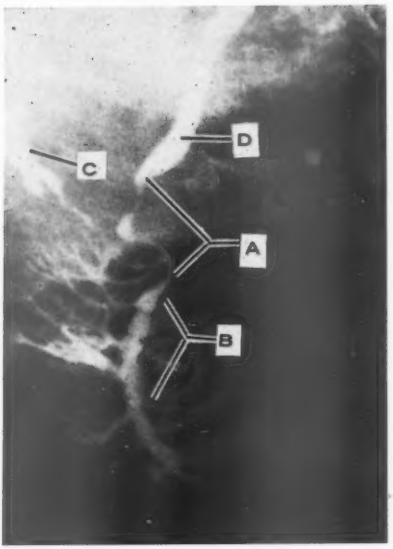

Fig. 4.—Sialogram showing tortuous constriction *(A)*, dilated main duct of gland with sausaging *(B)*, escape of dye into soft tissues posteriorly *(C)*, and dilation of Wharton's duct *(D)*.

SUMMARY

An interesting and unusual case of submaxillary duct obstruction from an invading carcinoma is reported. The sialographic changes are described and demonstrated.

Kings Highway and Church Ave.

ENDODONTICS

The American Association of Endodontists

Captain Warren J. Hedman, Editor

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A REVIEW OF THE DYNAMICS OF INFLAMMATION AS APPLIED TO THE DENTAL PULP

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THE starting place for a study of pulpal inflammation is with an irritant. Without an irritant, there is no inflammatory response. Basically, there are two types of irritants—viable and nonviable. Both induce a similar inflammatory response. The viable irritants differ from nonviable ones in that they bring with them additional biochemical substances which could alter the inflammatory response. The products of inflammation contain, also, certain irritant qualities.

Inflammation, "a disturbance of homeostasis," is a defensive chain reaction by the connective tissue elements, vascular and cellular, against an irritation. Therefore, it is important to understand the normal biochemistry of the pulp in order to comprehend the changes that occur with inflammation.

The elements involved in the inflammatory process—the irritant, the connective tissue, the inflammation itself, and repair—are influenced by a number of factors, including past inflammatory experience, nutrition, hormones, vitamins, state of health, age, etc., to mention a few.

DENTAL PULP

Morphologically, the dental pulp is composed of cells, fibers, and a ground substance, as well as a profuse blood supply. The blood, also a connective tissue, contains essentially the same physiologic elements as the pulp. The pulp also contains nerve fibers and probably lymphatics.

The formed elements of the dental pulp lie in a ground substance, which is a homogenous, transparent, gelatinous substance whose water content is held in a colloidal state. Chemically, this ground substance is a nitrogenous acidic polysaccharide conjugated with loosely held proteins with or without a sulfuric

acid molecule(s). The most important polysaccharides are (1) chondroitin sulfate, (2) mucoitin sulfate, and (3) hyaluronic acid. These substances are particularly hydrophilic and form viscous solutions which impart bulk to the dental pulp. The normal permeability of the pulp depends upon these polymers. They are also highly resistant to fluids as well as to particulate matter, including bacteria.

The mucopolysaccharides are vulnerable to depolymerization by enzymes which increase the permeability of the ground substance. These mucolytic agents are (1) hyaluronidase, which hydrolyzes hyaluronic acid, and (2) sulfamucase, which hydrolyzes chondroitin sulfate and mucoitin sulfate.

Other factors also regulate the ground substance. These are the vitamins and hormones which affect the permeability of the ground substance.

The vitamins influence enzyme systems. For example, vitamin C affects the colloidal condition of the matrix and fibers. The hormones affect the ground substance by increasing or decreasing its permeability. For example, estrone increases the quantity of the acid mucopolysaccharides and thereby decreases their diffusibility. Thyroxine also produces the same affect. Cortisone and progesterone reduce the quantity of the acid mucopolysaccharides. The hormones are important in inflammation, but their specific role in pulpal inflammation has yet to be evaluated.

Suspended in this ground substance are fibers which belong to a group known as the scleroproteins (albuminoid), which increases with advancing age. Hence, in an older pulp one would find more fibers and fewer cells. Of the three types of connective tissue fibers known, the dental pulp contains only the collagenous and reticular fibers, which seem to be alike chemically except that they differ in the stage of maturity. The younger of the two, reticular fibers, are particularly attractive to precipitated silver and are therefore referred to as argyrophilic fibers.

Also suspended in the ground substance of the pulp are a number of cellular elements. Aside from the cells comprising the capillaries and the nerves, the pulp contains undifferentiated mesenchymal cells, fibroblasts, macrophages, lymphoid wandering cells, and odontoblasts.

These cells are necessary to maintain the integrity of the entire tooth. They perform their function by producing biochemical agents. Basically, these agents are synthesized from the carbohydrates, proteins, lipids, minerals, and oxygen that are ingested and carried by the microcirculation.

THE INFLAMMATORY RESPONSE

With excessive stimulation, the cells and the matrix are damaged. This damage produces an increase in cell permeability. Cell permeability is not the only reaction to the irritant; the cell membrane could also rupture, allowing its contents to escape. On such occasions the escaping elements alter the permeability of the surrounding cells and the function of the immediate area. Farther away from the site of damage, the same elements that cause degeneration at the point of irritation are stimulatory to the more distant cells.

How does this increased permeability occur? Immediately on cell damage there is released a chemical substance which influences cell permeability. Experimental evidence shows that when cells are damaged hyaluronidase is liberated. It is believed that this chemical substance produces an increase in cell permeability. However, there are those who maintain that histamine or histamine-like substances are the factors involved in affecting cell permeability.

As this altered fluid exchange affects the cells of the dental pulp, it also affects the capillaries in a similar fashion. This chemical mechanism will cause a loss from the capillaries of plasma, salt, urea, fibrinogen, formed elements, lipids, mucin, antibodies, enzymes, antienzymes, and hormones. Further alterations are effected by the change in diameter of the blood vessels. The first change seen, which is initiated by the nervous system, is an instantaneous but brief contraction by these vessels. This is immediately followed by a longer-lasting dilatory phase, a chemically inspired alteration. Actually, the arterioles, metarterioles, and precapillary sphincters actively dilate, allowing more blood to flow through them and thence to the capillaries which now swell passively to accommodate this greater volume. The chemistry at this point involves the production of weak acids formed from the interaction of the water that is present and the overabundance of carbon dioxide (as carbonic acid). An additional factor contributing to the dilatation is a lack of oxygen caused by the stagnation of the blood flow. Products of injured cells, such as leukotaxine, hyaluronidase, histamine, platelet accumulation (liberating more histamine), all contribute as well to the dilatation of these affected vessels.*

The next change is the slowing of the blood stream immediately after a brief acceleration. This slowing allows time for the migration of the blood stream contents into the extracapillary spaces. If the slowing is marked, however, it can result in complete stasis with subsequent necrosis. The factors controlling this deceleration are swelling and proliferation of the endothelial cells and the increased stickiness and roughness of the endothelial walls. The increase in size of the endothelial wall is caused by the absorption of carbon dioxide and the acids of increased metabolism. This, in combination with protein, increases its hydrotropic properties producing swelling. Swelling also occurs in the protein of the plasma, thereby increasing its viscosity which also aids in slowing the blood stream.

Similarly, the erythrocytes absorb carbon dioxide and metabolic acids, causing them to swell and clump. As the current slows, the demarcation between the axial and peripheral zones becomes less distinct; in fact, the elements of each often blend.† The leukocytes, however, tend to gather along the periphery of the vessels or to marginate. This happens because of (1) the lighter weight of the erythrocytes, (2) the lower surface tension, and (3) the presence of leukotaxine. One of the important factors influencing this margination is chemotaxis. Chemotaxis is the reaction of certain cells to a stimulus, usually

*The diameter changes in the vessels can be controlled by manipulation of nervous impulses. When the constrictor is cut, inflammation proceeds at a normal rate; when the dilators are cut, necrosis ensues.

†In capillaries there are no zones; space exists for only one cell at a time.

the products of bacterial metabolism and/or the products of tissue breakdown. Leukotaxine is an example of a chemotactic substance which, according to Menkin, increases capillary permeability. Chemotaxis actually induces the migration of the white blood cells through the capillary wall. This movement of leukocytes serves two functions: (1) the ingestion of the invading bacteria, and (2) the providing of proteolytic enzymes, the important ones being pepsin, trypsin, and cathepsin.

With the escape of the contents from these affected blood vessels into the extracapillary spaces, there now exists an exudate. It is composed of two fractions:

1. *A lymphlike fraction* containing plasma, urea, fibrin-forming elements, lipids, mucin, antibodies, enzymes, antienzymes, and hormones.

2. *The formed-elements fraction* containing:

Polymorphonuclear leukocytes, which ingest bacteria by phagocytosis and remove solid particles of cell and tissue breakdown. These cells also provide proteolytic enzymes, such as pepsin, trypsin, cathepsin, and leukoprotease. Other enzymes present are lipase and glycosidases. With the exception of leukoprotease, these enzymes are liberated upon the death of the leukocyte. Their function is to liquefy injured cells and form pus. On the other hand, leukoprotease is active during the life of the cell. It is important to note that polymorphonuclear leukocytes appear early in inflammation and function only in an alkaline medium.

Macrophages, which become more numerous as the pH of the exudate changes to acid. Macrophages have the ability to group and form foreign body giant cells. They are mainly phagocytic and do the "mopping up" which prepares the area for repair. Lymphoprotease is the enzyme responsible for the digestion of the ingested particles in this cell type.

From the previous discussion, it is evident that pH is a factor of great influence during inflammation. It conditions the types of cells to be found in the exudate. The acidosis, in part, is a result of a fall in the alkaline reserve as well as the absence of oxygen. Mainly, however, the lower pH is due to the lactic acid produced by the anaerobic glycolysis of glucose.*

Lymphocytes, which are characteristic of chronic inflammation but rarely phagocytic. Their function is believed to be concerned with antibody formation. They appear together with *plasmacytes* which form the "round-cell infiltration" characteristic of chronic inflammation. McCrabb and Kelsey have shown that they also behave as trephocytes which synthesize and store nucleic and amino acids for use by other cells. These cells appear as the pH of the exudate turns acid.

*Because of the disruption of the normal flow of blood (oxygen), cells acquire their energy by an aerobic glycolysis.

Erythrocytes, whose function is to carry some oxygen to the cells of the exudate.

Platelets, which are found in small numbers in the dental pulp. Their function is obscure, but it is believed that they may (1) liberate fibrinogen, (2) help immobilize bacteria by their clumping action, and (3) plug injuries in small vessels.

Eosinophils, which are seen mostly in inflammations of the allergic type and are occasionally seen in the pulp.

Fibrinogen, which is a protein component of plasma and, with tissue damage and inflammation, coagulates to form fibrin. Fibrin appears early in the inflammatory process, again according to Menkin, as a response to leukotaxine. Its purpose is to fix the irritant mechanically, to allow time for the assemblance of leukocytes, and to form a network of roughened surface areas on which the polymorphonuclear leukocytes can phagocytose more efficiently. Later the fibrin begins to disappear as a result of the proteolytic action of the leukocytes.

One of the more important phases of the exudate is the role that phagocytosis plays in behalf of body defense. Actually, phagocytosis is promoted by the opsonins and tropins liberated through the increased permeability of the blood vessels. They form a film around the substances to be ingested, which alters the interfacial forces. Although a macrophage-promoting factor *(MPF)* has been reported, there seems to be a more central control for macrophage activity. According to Gordon and Kalish, the adrenal cortex influences the structure and function of the macrophages.

SUMMARY

The exudate has a manifold significance. It dilutes soluble poisons and irritants. It aids in the formation of fibrin. Its flow into the lymphatics helps disseminate soluble toxins. It affords an avenue of escape for catabolites formed in excess. Its enzyme content tends to neutralize bacterial products. Its proteolytic enzymes tend to dissolve injured and dead tissue.

It is the histologic character of the exudate that gives identification to the type of inflammation. We must remember that the type or phase of inflammation can change hourly. The definitive outline method of dividing pulpal inflammation into four types—acute suppurative, acute serous, chronic ulcerative, and chronic hyperplastic—is of little clinical value. Clinically, it is rarely possible to know which of these phases of inflammation predominates, since the whole picture is one of constant change.

Clinically, the best that we can do is to diagnose an inflammatory response as either acute or chronic. Even this is hazardous when we are dealing with the dental pulp, for both types may exist concurrently.

The use of the terms "acute" and "chronic" as applied to inflammation is merely a reference to time in that an acute inflammation is a new situation of

short duration whereas chronic inflammation is of long duration. *Severity* plays no part in this definition.

In acute inflammation the main histologic characteristics are those of exudation and the predominance of polymorphonuclear leukocytes. However, as time passes, the histologic picture changes. Exudation is lessened and the polymorphonuclear leukocytes are slowly replaced by lymphocytes and other chronic inflammatory cells. Chronic inflammation differs from this in that it is less degenerative but more proliferative. It is characterized by a fibrous thickening of a collagenous nature with vascularization in various stages of maturity. Present also are lymphocytes, plasmacytes, and macrophages. The inflammatory area exists in a state of flux, with certain elements resembling repair and others showing inflammatory characteristics. This condition could lead to total repair, regress to an acute (new) situation, or remain chronic indefinitely.

The stages cited above can affect either the entire dental pulp or any part of it. The prognosis for eventual repair is dependent largely on the intensity and the duration of the irritant.

Considering all the variables, an inflamed dental pulp could take one of several courses: (1) partial inflammation with attempts at repair, expressed either as a walling-off of the inflammatory process or actual calcification of the area after a fibrous infiltration, or inflammation involving the entire pulp, with or without necrosis; (2) total inflammation with attempts at repair or eventual necrosis; or (3) necrosis.

CONCLUSION

Inflammation is a characteristic pathologic phenomenon, common to all connective tissues in the body. The dental pulp, although a highly specialized organ, cannot be set apart from the normal actions and reactions of connective tissue. Each organ, while acting similarly in the process of inflammation demonstrates essentially a specificity only in repair.

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255 S. 17TH ST.

Section of the

FEDERAL DENTAL SERVICES

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LIPOMA, BENIGN TUMOR OF SOFT ORAL STRUCTURE

Report of a Case

S. L. Orlean, D.D.S., Philadelphia, Pa.*

ORAL lipomas are rather infrequent tumors. They are fatty tissue neoplasms which grow slowly and painlessly. The literature identifies the lesions with most areas of the oral cavity where adipose tissue is present—the tongue,[1] the oral vestibule,[2, 7] the maxilla,[4, 5] the lip,[3, 6] the mucosal surface of the cheek,[7] and the facial spaces.[5]

The following case is of interest because of the length of time that the lesion was present and because it was badly broken down teeth rather than the lesion which led the patient to seek treatment.

CASE REPORT

History.—A 65-year-old Negro man was admitted to the hospital on June 19, 1959, complaining of bad teeth and a swollen lip. The patient stated that the lip had been swollen for about eighteen years and was getting larger, that it was not painful, and that it did not interfere with his eating. He said that the teeth were bothering him, but not the lip. No history of trauma to the lip could be elicited.

Physical Examination.—The patient, a thin, well-nourished man, was alert and in no distress. On admission, his blood pressure, temperature, and pulse were within normal limits. Routine laboratory tests, including a complete blood count, urinalysis, and determination of bleeding and coagulation times were normal. The VDRL test was negative. Examination of other systems revealed noncontributory findings. There was an asymmetry of the lips (Fig. 1).

Intraoral Examination.—There were numerous decayed teeth and retained roots. In the lower right lip there was a large, soft, sessile mass within an intact mucous membrane of normal tone and color (Fig. 2). This mass was approximately 2 by 5 cm. at its greatest diameter. It was not ulcerated, indurated, or tender to palpation. On compression, it felt like soft putty.

*Chief, Dental Service, Veterans Administration Hospital, Philadelphia, Pennsylvania; Associate in Oral Medicine, University of Pennsylvania School of Dentistry.

Radiographic Examination.—Periapical films revealed numerous radiolucent areas at the apices of the decayed teeth and retained roots. A radiograph of the lesion was lacking in detail.

In view of the clinical findings, no biopsy and/or aspiration biopsy was attempted. Excisional biopsy was the treatment of choice.

The clinical impression was that the mass in the lip was either a lipoma or a mucous retention cyst.

Fig. 1.—Asymmetry of lips.

Fig. 2.—Mass in lower lip and oral mucosa.

Treatment.—On June 29, 1959, after the right mandible was anesthetized with Xylocaine hydrochloride with epinephrine 1:100,000, six right mandibular teeth were removed, an alveolectomy was performed, and the tissues were coapted with 4-0 silk ligature. The mucous membrane was incised over the labial lesion. By careful dissection, the thick

capsule surrounding the growth was exposed and separated from the attached mucous membrane. The mass was firmly adherent to the underlying tissue at only one point. A small amount of excess tissue was removed from the edges of the incision. The edges were sutured with 4-0 silk ligature. During the procedure no fluid was expressed from the mass.

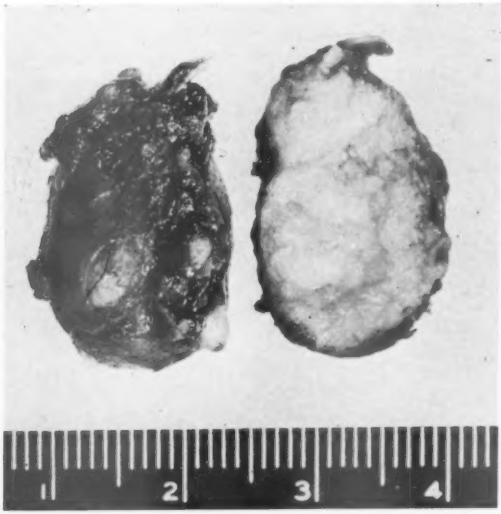

Fig. 3.—Gross specimen. Note lobulated, glistening surface.

Fig. 4A.—Microscopic section, ×28. *(Fig. 4B on opposite page.)*

Postoperative Course.—The patient did well, and healing was uneventful. The sutures were removed on July 8, 1959. Distortion of the lower lip was minimal (Fig. 5).

Pathologist's Report.—

Gross: The specimen consisted of a soft encapsulated nodule measuring 2 cm. at its greatest diameter, with a small portion of mucous membrane attached at one area. The cut section revealed a homogeneous mass, slightly lobulated, with a yellowish glistening surface (Fig. 3).

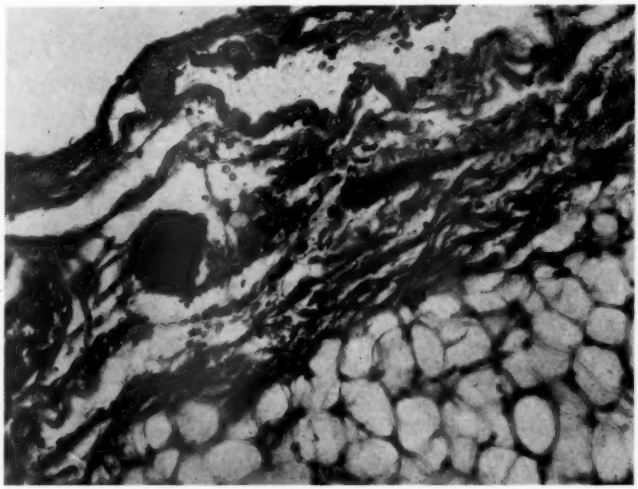

Fig. 4*B*.—Microscopic section, ×180.

Fig. 5.—Four weeks after operation. Note symmetry of lips.

Microscopic: Sections showed an encapsulated, lobulated collection of fatty tissue. There was a small fragment of stratified squamous epithelium at one portion. Two small nodules of salivary gland and duct were seen. No evidence of malignancy was found in the specimen (Fig. 4).

SUMMARY

A case of lipoma of the lip and oral mucosa is presented. This benign neoplasm had been present for approximately eighteen years, growing slowly and painlessly. It was composed of adult fatty tissue, and it was lobulated and well encapsulated.

Appreciation is expressed to Dr. Charles F. Mallon who replaced the patient's dentition with a complete denture prosthesis.

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AN EVALUATION OF CARBOXYMETHYL CELLULOSE AS AN ABSORBABLE COAGULANT IN ORAL SURGICAL PROCEDURES

Irwin W. Scopp, B.S., D.D.S., Harry Fredrics, B.A., D.D.S.** and Jerome Dean Anderson, D.D.S.,*** New York, N. Y.*

THE purpose of undertaking a study involving a hemostatic agent is to continue the search for a material which will more nearly approach the ideal in its working features. Hemostasis is important primarily because the retention of vital whole blood prevents shock and stress on the cardiovascular system. Also, good hemostasis permits ease in operating, since the field is clear and tissues are thus better differentiated.

The ideal hemostatic agent is easily detoxified and absorbed by body fluids, it is manipulated without difficulty, and it acts by either vasoconstriction or coagulation.

Hemostasis is not practiced with any one ideal agent. Thromboplastin containing a phospholipid, fibrinogen, viper venom, and epinephrine are some of the solutions used and applied topically. Although they are of great value, these agents are difficult to manipulate, especially when large hemorrhagic fields exist. Pressure packs, Gelfoam, and gelatin sponges are applied directly to sockets and bleeding areas, but they are kept in position with some difficulty and may contribute to postoperative complications.

Carboxymethyl cellulose† cones are made from especially pure sodium carboxymethyl cellulose converted to the free acid compound, namely, modified carboxymethyl cellulose, which is then purified further and compressed into a tablet or dental cone. The structural formula is shown in Fig. 1. Carboxymethyl cellulose produces hemostasis by (1) reacting with the blood to form a gelatinous coagulum that blocks several blood vessels and (2) swelling upon contact with blood, so that additional hemostasis is achieved.‡

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***Resident in Oral Surgery, Veterans Administration Hospital, New York, New York.

†Modified carboxymethyl cellulose is manufactured under the trade-mark "Surgicel" by Johnson & Johnson, New Brunswick, New Jersey.

‡Personal communication received from J. Morgan Macom, Jr., D.D.S., Assistant Director of Clinical Research (Dental), Johnson & Johnson, and Mr. C. E. Moser.

The purpose of our evaluation was to determine the usefulness of modified carboxymethyl cellulose as an absorbable cone in the control of bleeding problems following oral surgical procedures of the following categories:

1. Routine exodontia and complex exodontia
   (a) Impactions
   (b) Removal of residual roots
2. Alveolectomies
3. Cystectomies
4. Multiple tooth extractions under general anesthesia
5. Exodontia as an emergency procedure in patients undergoing Dicumarol therapy
6. Intermediate or secondary hemorrhage
7. Oral surgical procedures in patients with a "bleeding" history
8. Oral surgical procedures in patients with a history of essential hypertension

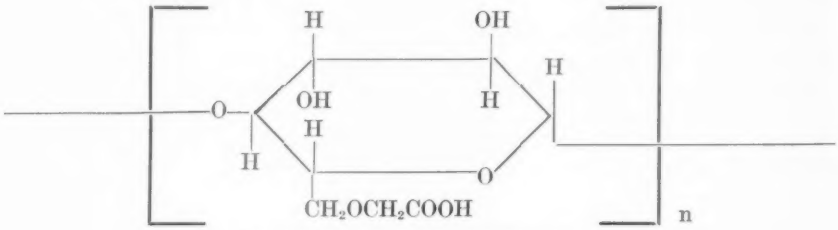

Fig. 1.—Modified carboxymethyl cellulose.

A double-blind technique was employed. The patient's history and general physical condition were noted on a prepared work sheet. The procedure performed was noted, and modified carboxymethyl cellulose cones were placed in the surgical field. The amount of bleeding was noted at five-minute intervals for twenty minutes, and then at twelve-hour intervals for four days. Evidences of foreign-body reactions were recorded. Two other hemostatic agents (specially treated gelatin and oxidized cellulose) were used for purposes of comparison and control. The third control, containing no agent, was maintained wherever multiple sockets or cavities existed after surgery.

A total of sixty-two patients were included in the study. Of these, twelve served as controls. In every case in which multiple extractions were performed, the patient served as his own control, one or two sockets being treated with only a 2 by 2 inch gauze pack held in place over the sockets with occlusal pressure.

In the experimental group, an experimental cone was placed in each socket immediately after extraction. The ease with which the cone was handled was realized when it was found that any tissue forceps or College pliers could grasp the cone and position it completely into the socket. The cone is somewhat oblong and tear shaped with a thickness of 3.5 mm.

The time involved in controlling bleeding was then recorded. In 80 per cent of the experimental group, the time required for complete apparent arrest of hemorrhage was 1.7 minutes. In the control group, apparent cessation of bleeding occurred at around the normal bleeding time of three minutes. Those sockets packed with specially treated gelatin and oxidized cellulose stopped hemorrhaging somewhat beyond two minutes. This may have been due to difficulty in placing the agents. As soon as it was completely absorbed with blood, the pellet-shaped control became difficult to manipulate and tended to rise from the individual socket. The Gelfoam square had to be trimmed to fit each socket, which made it somewhat less effective, and it kept adhering to the forceps as it was placed. It should be noted that too much manipulation, extraorally and intraorally, before the agent is placed will destroy its sterility.

Postoperative bleeding was checked every five minutes for twenty-minute periods in all cases involved in the project. The patients were then observed twelve hours later and again each day for four days. Observations were made in some cases by an investigator other than the patient's surgeon in order to minimize biased impressions.

No intermediate or secondary hemorrhage occurred in any of the experimental group. After twenty-four hours the sockets appeared well clotted, with a slightly raised oval lid which, on examination, was found to be the modified carboxymethyl cellulose in a crumbly soft mesh with clot formation adhering. Two days later, the clots were retracted into the socket and felt firm. The usual color was a dark red with a dull cast, indicating that the clot was organizing. In comparison, the sockets treated without the hemostatic agent were filled with a friable red mass for thirty-six hours before the material retracted into the socket. Slight oozing was apparent in seven patients of the control group after thirty-six hours, and two patients continued to show slight oozing of blood after forty-eight hours.

In the group of patients with predictable or expected postoperative hemorrhaging, the results imply that the carboxymethyl cellulose cone greatly assisted in clot formation. Four patients undergoing Dicumarol therapy one week prior to exodontia manifested no hemorrhage and developed solid clots during the same time intervals as patients who were not under Dicumarol treatment. One patient was treated, without any postoperative precautions, under emergency conditions in which two painful and carious teeth were removed. Two days after the extractions the patient began hemorrhaging intermittently and was brought to the dental clinic, where two carboxymethyl cellulose cones were placed in the molar socket and one was placed in the premolar socket of the maxilla. Bleeding was arrested in less than three minutes, after which sterile packs were maintained over the sockets with occlusal pressure. The patient was observed for four succeeding days, during which no recurrence of hemorrhage was evident. Healing of the sockets was uneventful.

Surgical flap procedures were augmented wherever possible with carboxymethyl cellulose cones. As many as three cones were placed into socket

areas both in third molar impaction areas and in other areas where the procedures involved removal of residual or retained roots. Where cystectomies had been performed, the cavities created were filled with cones that had been pulverized in order to create better adaptation to the cavity walls.

Patients with a "bleeding history" which had not been substantiated by laboratory data fared well with the use of carboxymethyl cellulose cones, as well as with the control agents. Bleeding histories without definite medical and laboratory histories are usually vague recollections on the part of the patient, and most often there is no substantiation. However, every patient with such complaints must be studied thoroughly to determine whether any basis for a bleeding problem exists. In almost all instances patients with extreme problems, such as the leukemias and related blood dyscrasias, should not be considered candidates for exodontia. Mechanical aids applied topically are not substitutes for premedication and are not intended to give the operator a false sense of security where there are contraindications to surgery because of the prospect of massive hemorrhage or infection.

Fortunately, failures and complications remained at a minimum with the use of the experimental cone. In only one case of postoperative blood oozing after insertion of the experimental cones was there any need to resort to other means to control hemorrhage. In this case suturing was performed to close the socket opening with mucosa corrected. The oozing was controlled immediately and no further difficulty was encountered. Subsequent laboratory data revealed a good prothrombin time and a negative hemogram for this patient. It is possible that the socket may have been either contaminated by the cone or traumatized by the patient in some manner.

The diagnosis of "dry socket" was made in one case in which the carboxymethyl cellulose cone was used. This patient had informed the surgeon of a history of postoperative bleeding following tooth extraction, and a cone was placed in the socket of the mandibular second premolar. The socket had been moderately traumatized when a retained root was removed with gouge elevators. Two days postoperatively the patient complained of extreme pain, and examination revealed that the gingival tissue was ecchymotic and somewhat retracted from the bony socket. The cone was curetted and the patient was placed on dry socket therapy consisting of daily administration of paramethyl guaiacol. The course of events was typical for this condition, with the patient receiving only moderate relief for about five days until the symptoms were markedly lessened.

DISCUSSION

1. Carboxymethyl cellulose produces hemostasis by reacting with hemoglobin to form a coagulum which swells on contact with blood to exert a pressure on the surrounding blood vessels.

2. Since the material is completely absorbable, the need for subsequent observations is eliminated.

3. The indications for carboxymethyl cellulose hemostasis may be summarized as follows:

(a) Postoperative control of bleeding after exodontia.

(b) Extensive alveolectomy in conjunction with a proper suturing technique.

(c) In cystectomies, where the cavity remaining is of moderate size, the cones may be pulverized and inserted, both for hemostasis and to support overlying tissue against collapse.

(d) Intermediate or secondary hemorrhage, if hemorrhage is not subsequent to serious blood dyscrasias.

(e) Any surgical intervention requiring flap procedures. The cone seems to give support to overlying tissue, as well as producing hemostasis.

4. The only contraindication to the use of carboxymethyl cellulose cones is the existence of acute infections in the operative field. Since such areas may have poor circulation and tissue resistance to trauma and organisms, the addition of a foreign body would serve no apparent purpose.

SUMMARY

1. The administration of carboxymethyl cellulose cones for postoperative hemostasis was effective in almost all cases.

2. Postoperative complications were nonexistent except in one case. It is suggested that the cones be manufactured in several sizes to accommodate the smaller sockets of anterior teeth.

3. The cones do not cause any discomfort to the patient and they help to allay apprehension when he is informed of their purpose.

4. No systemic side effects from the use of carboxymethyl cellulose were observed. The basic chemical formula of this material has been used in many forms, both in contact with body tissues and as an ingredient of certain foods.

CONVERSION OF A DENTAL CHAIR TO AN OPERATING TABLE

Russell A. Conway, Technical Sergeant, USAF, and*
*Gilbert A. Koehler, Captain, USAF (DC)***

THE advantages of having the patient in a supine position for oral surgery procedures are numerous. This position considers accepted physiologic principles, and there is no syncope. Once an operator becomes accustomed to performing oral surgery procedures on patients who are lying down, he will prefer this to any other method.

Necessity, the mother of all invention, has led to the use of a standard dental chair to meet the oral surgeon's need for a practical operating table that is immediately available. The conversion from chair to table is an economical one, which can be made at a cost of $20.00 for carpenter's labor and materials. (A standard operating table costs from $850.00 to $1,900.00.) The table can be reconverted to a chair in thirty minutes. Since the pedestal of a standard dental chair is used, the operating table can be raised to any desired height, it can be tilted, and it can be lowered more than a standard operating table. Also, there is excellent acceptance by the patient.

First, the back seat and the foot-rest assembly are removed from the base of the dental chair. In the back portion of the cushion frame are three bolts which hold the back-rest adjustment bracket; the center bolt is now removed. When the chair has been thus stripped, measurements may be taken for the sturdy wooden frame that is to be mounted on the base (Fig. 1). For a full range of tilting adjustments, the cushion frame should be tilted back three notches and a 3 inch cross-member shim should be constructed on the rear portion of the frame; without it, the foot of the table cannot be tilted downward. The frame is made of two 2 by 8 inch planks approximately 6 feet long, connected by four 2 by 4 inch pieces of wood 22 inches long. When the framework is completed, it should be stabilized with bolts run through the holes that originally held the foot rest to the cushion frame. Another bolt should be used on the rear portion of the cushion frame. This bolt is passed through the 3 inch cross-member shim via the hole for the bolt that originally held the back-rest bracket. This will provide adequate stabilization of the framework to the base of the chair.

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*Noncommissioned officer in charge of Dental Clinic.
**Technical advisor, oral surgeon, Chief of Dental Services.

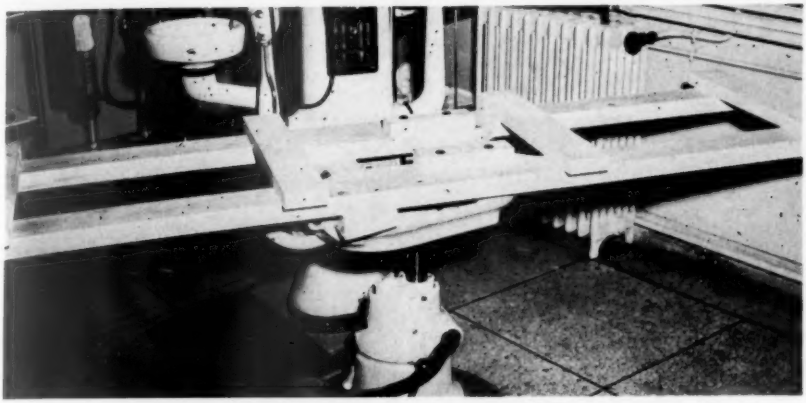

Fig. 1.—Dental chair with framework completed.

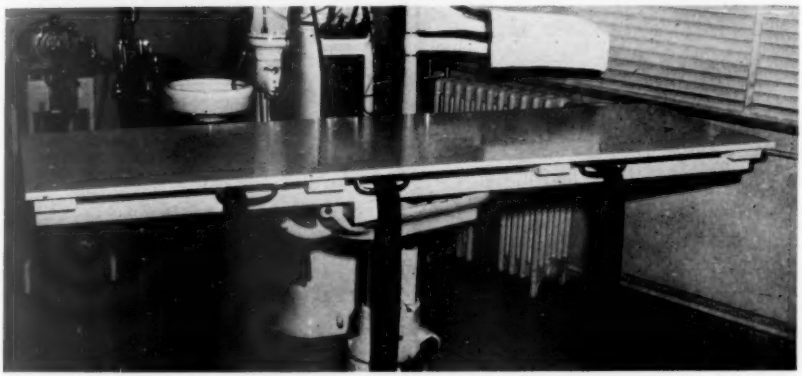

Fig. 2.—Operating table top completed. Three of the six handles, with litter straps, are shown.

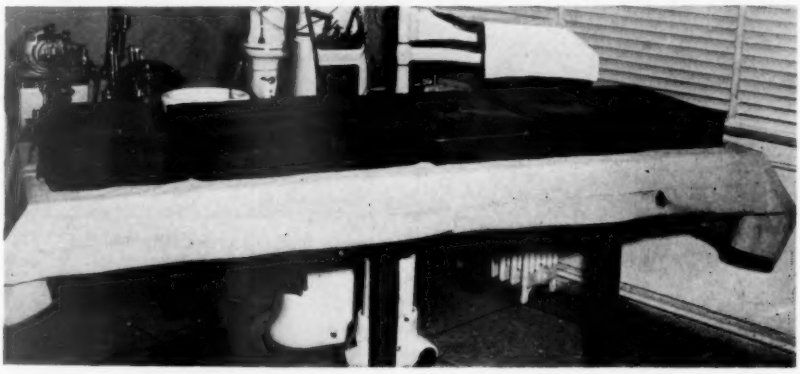

Fig. 3.—Table padded with standard operating table cushion.

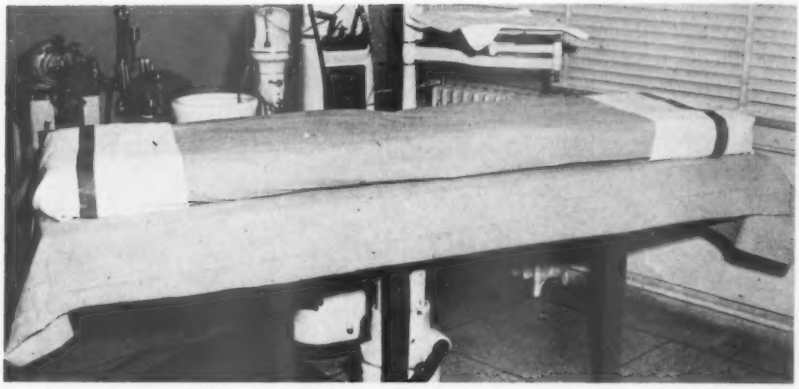

Fig. 4.—Operating table draped and ready for use.

Fig. 5.—Operating table tilted so that patient's feet are lower than his head.

The top of the operating table is made of ¾ inch plywood and firmly attached to the frame. Fig. 2 shows the completed table top. The legs of a Mayo stand will straddle the pedestal base.

Fig. 6.—Operating table tilted so that patient's head is much lower than his feet.

Ideally, the operating table should be padded with a standard operating table cushion (Fig. 3). However, a regular examining table mattress can be used. When ready for use, the table should be draped as shown in Fig. 4.

Figs. 5 and 6 illustrate two of the tilted positions that may be obtained with this table.

BENIGN INTRAORAL HEMANGIOPERICYTOMA

Report of a Case

*Martin F. Anderson, Captain, DC, USA**

In 1942, Stout and Murray[1] published a study of nine tumors and suggested the name *hemangiopericytoma*. In 1949, twenty-five cases of this tumor were gathered by Stout[2] from various localities in North America. At that time it was felt that this number constituted a clinical and pathologic entity.

The clinical data compiled in this series showed that there was no sex predilection and that there was a relatively even age spread from birth to 81 years. The anatomic distribution of these tumors seemed to be as wide as the distribution of capillaries. In the survey there was only one intraoral tumor, there were two tumors associated with the head and neck, and the remainder were removed from various other sites. In 1956, Stout,[3] in a symposium, had enlarged his series to include twelve intraoral lesions.

Histologically, the tumor is complex and demonstrates great variation. The cells are not uniform in size or shape; neither is there any uniformity in the amount and distribution of connective tissue fibers. Essentially, the tumor consists of capillaries lined with normal endothelial cells and surrounded by tumor cells. On occasion the blood vessel would be difficult to detect because of the large number of tightly packed tumor cells. The question obviously arises as to whether one is dealing with a hemangioendothelioma or a hemangiopericytoma. This is quickly determined by the use of a silver reticulin stain, which readily demonstrates the tumor cell to be perivascular.

The characteristic cell of the tumor is rounded or elliptical. Murray[1] cultured these cells and demonstrated long branching processes; these cells were essentially the "pericytes" described by the Swiss histologist, Zimmermann.[5] Although these cells have no myofibrils, they possess contractile powers. Stout assumed that there was a relationship to smooth-muscle cells.

CASE REPORT

A 48-year-old Filipino man was observed clinically at Letterman General Hospital in early 1959. His chief complaint was spontaneous bleeding from an edentulous area of the mandibular arch distal to the right cuspid. There was no discomfort associated with this, and the hemorrhage had occurred on three separate occasions in the past two weeks.

From Letterman General Hospital, San Francisco, California.
*Present address: Department of Oral Surgery, Fort Campbell, Kentucky.

Oral examination revealed a fresh clot that occupied the buccal sulcus. This was carefully removed without causing fresh bleeding. The oral examination was essentially negative except for a slightly spongy, dark red area on the crest of the ridge. The nature of the lesion caused me to regard it as being a foreign body reaction. There was no evidence of purulent matter associated with the lesion, however, and roentgenographic evidence was negative. Therefore, an exploratory procedure was performed.

A superficial incision along the crest of the ridge was made through the gingiva. At a point above the periosteum, a line of cleavage was encountered. Soft tissue was bluntly dissected to a point at which the lesion now appeared encapsulated. The tumor was removed without excessive bleeding. The removal was considered complete in all parts except at the most anterior part where the fibers of the periosteum, the periodontal membrane of the cuspid, and the tumor blended together into a single tissue.

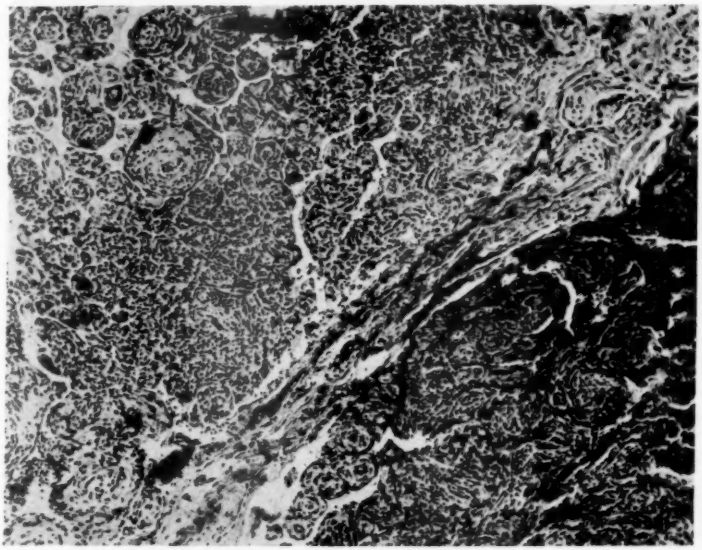

Fig. 1.—Low-power photomicrograph shows a section of connective tissue separating the tumor. (Hematoxylin and eosin stain.)

The specimen was submitted to the Pathology Department at Letterman General Hospital, and the following report was received:

Gross: The specimen consists of a roughly tear-shaped portion of mottled tan and brown tissue, measuring 1.3 by 0.6 by 0.3 cm. The cut surface is pale gray and fibrous in appearance. The specimen is hemisected and embedded as a single block.

Microscopic: The lesion is composed of many large and small vascular channels which are lined with several layers of plump endothelial cells, without any malignant characteristics. The pattern is somewhat unusual in that many of these proliferating vascular channels may be found within some of the larger spaces, suggesting a somewhat papillary pattern (Fig. 1). The proliferating endothelial cells are seen at the margin of excision (Fig. 2).

Diagnosis: Soft tissue from alveolar ridge; hemangioendothelioma, benign.

Later, when this tissue was received at the Armed Forces Institute of Pathology, the staff altered this diagnosis and coded the specimen in their files as hemangiopericytoma.

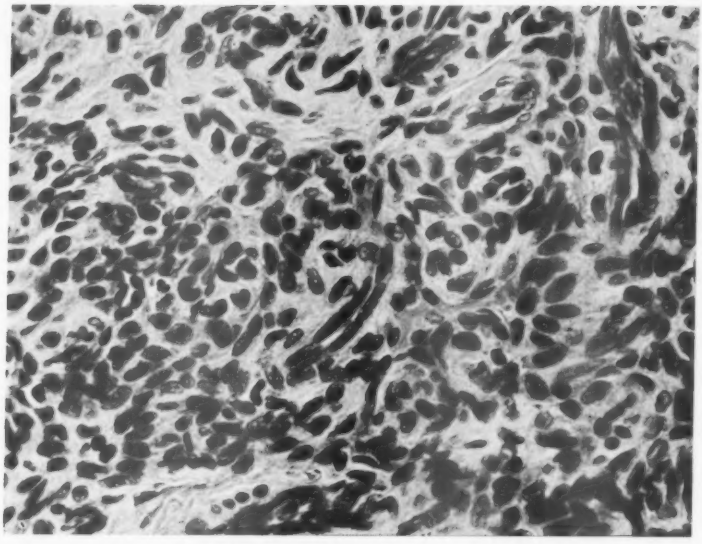

Fig. 2.—High-power photomicrograph of tumor. The capillaries are lined by normal endothelial cells. Surrounding the lumina are the rounded or elliptical tumor cells. (Magnification, ×430.)

SUMMARY

A case of hemangiopericytoma of the oral mucosa in a 48-year-old man is reported.

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ANNOUNCEMENTS

International Conference on Oral Surgery

The first International Conference on Oral Surgery, sponsored by the American Society of Oral Surgeons in conjunction with the Royal College of Surgeons of England, will be held at the Royal College in London, July 1 to 4, 1962. All interested dentists and physicians are invited to attend. Visitors attending the Conference will have an opportunity to observe surgical procedures in the hospitals of London as a part of the Conference program.

For additional details and bulletin, dentists and physicians in the United Kingdom and Europe should write Dr. Terence Ward, c/o Royal College of Surgeons, Lincoln's Inn Fields, London, W. C. 2, England. Dentists and physicians in the United States and other countries should write Mr. D. C. Trexler, American Society of Oral Surgeons, 840 N. Lake Shore Dr., Chicago, Illinois.

First District Dental Society

The following postgraduate courses will be presented:

Preparation of Teeth for Jackets for Abutment Purposes. Oct. 5 to 7, 1961. Dr. I. Franklin Miller.

Newer Concepts in Restorative Dentistry. Oct. 18 and 19, 1961. Dr. Alexander Leff.

Occlusal Adjustment—Integration Into the Practice of Dentistry. Oct. 18, 1961. Dr. Julius N. Obin.

Oral Dynamics. Oct. 19 to 21, 1961. Dr. John T. McSweeney.

Horizontal Pinsplinting of Anterior Teeth. Oct. 27 and 28, 1961. Drs. A. J. Feldman and Carl Sanell.

All classes will be held from 10 A.M. to 4:30 P.M., unless otherwise noted, at the Statler-Hilton Hotel, Seventh Ave. at West 33rd St., New York, New York.

For further information, please write to the First District Dental Society, Statler-Hilton Hotel, New York 1, New York.

American Association of Audio Analgesia

The Association will hold a meeting at the New York Academy of Sciences, 2 East 63rd St., New York City, at 8 P.M. on Monday, Oct. 9, 1961. Dr. Aaron A. Moss will lecture, and Dr. Jerome S. Mittelman will act as discussant.

Further information may be obtained by writing Dr. Jerome S. Mittelman, 30 East 60th St., New York 22, New York.

Mid-Continent Dental Congress

The Mid-Continent Dental Congress will be held Oct. 29 to Nov. 1, 1961, at the Chase Hotel in St. Louis, Missouri. The following papers will be presented:

Monday, October 30

Some Aspects of the Dental Research Program at the National Bureau of Standards. George C. Paffenbarger, D.D.S., Washington, D.C.

X-ray Diagnosis in the Dental Office. William E. Koch, Jr., D.D.S., St. Louis, Missouri.

Call the Next Witness for the Defense—Legal Aspects of Dentistry. Richard F. Rabe, D.D.S., J.D., Des Moines, Iowa.

Conservation of Tooth Substance in the Preparation of Bridge Abutments. Roland W. Dykema, D.D.S., Indianapolis, Indiana.

Tuesday, October 31

Periodontia: A Part of Every Practice. Lloyd J. Phillips, D.D.S., Indianapolis, Indiana.

Treatment of Emergencies in the Dental Office. Robert E. Allen, D.D.S., M.S., Kansas City, Kansas.

The Problem of the Loose, Uncomfortable Denture. Bernard Jankelson, D.M.D., Seattle, Washington.

Wednesday, November 1

The Control of Pain in the Dental Office. Norman H. Olsen, D.D.S., M.S.D., Chicago, Illinois.

Communication—The Secret to Successful Human Relations. Stanleigh B. McDonald, B.S., Indianapolis, Indiana.

For complete details, write to Greater St. Louis Dental Society, 8013 Maryland Ave., Clayton 5, Missouri.

American Dental Society of Anesthesiology

The Society will hold its annual meeting on Oct. 13, 14, and 15, 1961, at the Statler-Hilton Hotel, New York, New York.

Austrian Dental Society

The Austrian Dental Society will observe its one-hundredth anniversary with a meeting in Vienna, Nov. 14 to 18, 1961. Further information may be obtained by writing to Dr. Harald Kränzl, General Secretary, Langegasse, Vienna, VIII, Austria.

Albert Einstein College of Medicine Yeshiva University

The Postgraduate Dental Program will sponsor courses in anesthesiology, endodontics, oral pathology, oral surgery, orthodontics, periodontics, pharmacology, clinical photography, and prosthetics during the 1961-62 academic year.

For further information and application, please write to Director, Postgraduate Dental Program, Albert Einstein College of Medicine, Eastchester Rd. and Morris Park Ave., Bronx 61, New York.

Oral Surgery Residency at Baroness Erlanger Hospital

A one-year approved oral surgery residency is available immediately at The Baroness Erlanger Hospital in Chattanooga, Tennessee.

Additional information may be obtained from Dr. Charles Landis, Sr., Director, Department of Oral Surgery, The Baroness Erlanger Hospital, Chattanooga 3, Tennessee.

American Academy of Oral Roentgenology

The annual scientific meeting of the Academy will be held at the Warwick Hotel in Philadelphia, Pennsylvania, on Saturday, Oct. 14, 1961. This meeting will be preceded on October 13 by an open Executive Committee meeting at which the affairs of the Academy will be discussed.

Boston University

The following postgraduate courses are offered by the Department of Stomatology, School of Medicine, Boston University and the Massachusetts Memorial Hospitals:

Occlusal Adjustment. Oct. 30 to Nov. 3, 1961. Drs. Bernard S. Chaikin, Henry M. Goldman, Gerald M. Kramer, William Pendergast, Irving Romanow, J. David Kohn, David J. Baraban, Leo Talkov, David V. Berry, and Jack Bloom. Fee, $200.00.

Periodontal Therapy. Nov. 6 to 10, 1961. Drs. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Irving Romanow, Jack Bloom, and associates. Fee, $200.00.

Endodontics. Nov. 13 to 17, 1961. Dr. Herbert Schilder. Fee, $175.00.

Fixed Bridge Prosthesis. Nov. 27 to Dec. 1, 1961. Drs. Leo Talkov, David J. Baraban, and Lloyd Warshauer. Fee, $175.00.

Periodontal Pathology. Jan. 22 to 26, 1962. Drs. Henry M. Goldman and Jack Bloom. Fee, $200.00.

The Use of Ultrasonics in Periodontal Therapy. March 17, 1962. Dr. Henry M. Goldman. Fee, $35.00.

Periodontal Therapy. March 19 to 23, 1962. Drs. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. Fee, $200.00.

Advanced Course in Periodontal Therapy. March 26-30, 1962. Drs. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, and associates. Fee, $200.00.

Apicoectomy—Surgical Endodontic Procedures. April 2 to 6, 1962. Dr. Herbert Schilder. Fee, $175.00.

Treatment Planning Clinic—Restoration of Missing Teeth. April 6 and 7, 1962. Staff, Department of Stomatology. Fee, $60.00.

Surgical Procedures in Periodontal Therapy. April 30 to May 4, 1962. Dr. Lewis Fox and associates. Fee, $200.00.

Full Mouth Reconstruction. May 14 to 18, 1962. Drs. Leo Talkov, David J. Baraban (Restorative Phase), Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, J. David Kohn (Periodontal Phase). Fee, $200.00.

For applications, write to David J. Baraban, D.M.D., Director of Postgraduate Studies, Department of Stomatology, Massachusetts Memorial Hospitals, 750 Harrison Ave., Boston 18, Massachusetts.

Temple University

A one-day course in clinical endodontics will be given at the School of Dentistry on Friday, Oct. 20, 1961, immediately following the annual meeting of the American Dental Association. The course is under the direction of Dr. Leonard Parris. Luncheon will be included. The fee for the course is $35.00.

For further information, write Dr. Louis Herman, Director of Postgraduate Studies, Temple University School of Dentistry, 3223 North Broad St., Philadelphia 40, Pennsylvania.

REVIEWS OF THE LITERATURE

BOOK REVIEW

Synopsis of Oral Pathology. S. N. Bhaskar, B.D.S., D.D.S., M.S., Ph.D., Major, United States Army Dental Corps; Chief, Oral Tumors Branch, Armed Forces Institute of Pathology; Assistant Professor of Oral Pathology, Georgetown University School of Dentistry. St. Louis, 1961, The C. V. Mosby Company. 502 pages. Price, $9.75.

For some time the need for an oral pathology text dealing solely with the gross and microscopic changes of disease has been recognized. All previous texts have combined pathology with treatment. This posed the obvious disadvantages of insufficient detail or difficulty in finding the desired information.

Dr. Bhaskar has written a thoughtful, well-organized book which is, indeed, a synopsis of oral pathology. The style is simple and to the point, and the author employs expressions which are clear and concise. Illustrations, both clinical and microscopic, are numerous; the microphotographs are generally good and the clinical photographs are, on the whole, poor. While not extensive, the references are ample.

The first part of the text is entitled "A Diagnostic Classification of Oral Pathology." This consists of a number of charts which group oral lesions by their most striking clinical characteristics, such as white lesions, vesicular lesions, ulcerations, etc. The arrangement is orderly and logical, and this entire section serves as a point of orientation and reference for clinical diagnosis and treatment of the various oral diseases. The major portion of the book employs the usual format for the presentation of pathology.

While this book is less than perfect, it is a giant step in the right direction. It is hoped that Dr. Bhaskar will complement this by a more detailed text which will serve as a reference for the pathologist and a text for the advanced student in oral pathology.

I would recommend this book, without reservation, as an aid in teaching oral pathology to the undergraduate dental student.

Jack Bloom.